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CANCER ASSOCIATED NUCLEIC ACIDS AND POLYPEPTIDES

**Field of the Invention**

The invention relates to nucleic acids and encoded polypeptides which are cancer associated antigens expressed in patients afflicted with breast cancer. The invention also relates to agents which bind the nucleic acids or polypeptides. The nucleic acid molecules, polypeptides coded for by such molecules and peptides derived therefrom, as well as related antibodies and cytolytic T lymphocytes, are useful, *inter alia*, in diagnostic and therapeutic contexts.

**Background of the Invention**

The mechanism by which T cells recognize foreign materials has been implicated in cancer. A number of cytolytic T lymphocyte (CTL) clones directed against autologous melanoma antigens, testicular antigens, and melanocyte differentiation antigens have been described. In many instances, the antigens recognized by these clones have been characterized.

The use of autologous CTLs for identifying tumor antigens requires that the target cells which express the antigens can be cultured *in vitro* and that stable lines of autologous CTL clones which recognize the antigen-expressing cells can be isolated and propagated. While this approach has worked well for melanoma antigens, other tumor types, such as epithelial cancers including breast and colon cancer, have proved refractory to the approach.

More recently another approach to the problem has been described by Sahin et al. (*Proc. Natl. Acad. Sci. USA* 92:11810-11813, 1995). According to this approach, autologous antisera are used to identify immunogenic protein antigens expressed in cancer cells by screening expression libraries constructed from tumor cell cDNA. Antigen-encoding clones so identified have been found to have elicited an high-titer humoral immune response in the patients from which the antisera were obtained. Such a high-titer IgG response implies helper T cell recognition of the detected antigen. These tumor antigens can then be screened for the presence of MHC/HLA class I and class II motifs and reactivity with CTLs

The invention is elaborated upon in the disclosure which follows.

### Summary of the Invention

Autologous antibody screening has now been applied to cancer using antisera from cancer patients. Numerous cancer associated antigens have been identified. The invention provides, *inter alia*, isolated nucleic acid molecules, expression vectors containing those molecules and host cells transfected with those molecules. The invention also provides isolated proteins and peptides, antibodies to those proteins and peptides and CTLs which recognize the proteins and peptides. Fragments including functional fragments and variants of the foregoing also are provided. Kits containing the foregoing molecules additionally are provided. The foregoing can be used in the diagnosis, monitoring, research, or treatment of conditions characterized by the expression of one or more cancer associated antigens.

Prior to the present invention, only a handful of cancer associated genes had been identified in the past 20 years. The invention involves the surprising discovery of many genes, some previously known and many previously unknown, which are expressed in individuals who have cancer. These individuals all have serum antibodies against the proteins (or fragments thereof) encoded by these genes. Thus, abnormally expressed genes are recognized by the host's immune system and therefore can form a basis for diagnosis, monitoring and therapy.

The invention involves the use of a single material, a plurality of different materials and even large panels and combinations of materials. For example, a single gene, a single protein encoded by a gene, a single functional fragment thereof, a single antibody thereto, etc. can be used in methods and products of the invention. Likewise, pairs, groups and even panels of these materials can be used for diagnosis, monitoring and therapy. The pairs, groups or panels can involve 2, 3, 4, 5... to as many as 25, 50, 100 or more genes, gene products, fragments thereof or agents that recognize such materials. A plurality of such materials are not only useful in monitoring, typing, characterizing and diagnosing cells abnormally expressing such genes, but a plurality of such materials can be used therapeutically. An example of the use of a plurality of such materials for the prevention, delay of onset, amelioration, etc. of cancer cells, which express or will express such genes prophylactically or acutely. Any and all combinations of the genes, gene products, and materials which recognize the genes and gene products can be tested and identified for use according to the invention. It would be far too lengthy to recite all such combinations; those skilled in the art, particularly in view of the teaching contained herein, will readily be able to determine which combinations are most appropriate for which circumstances.

As will be clear from the following discussion, the invention has *in vivo* and *in vitro* uses,

including for therapeutic, diagnostic, monitoring and research purposes. One aspect of the invention is the ability to fingerprint a cell expressing a number of the genes identified according to the invention. Such fingerprints will be characteristic, for example, of the stage of the cancer, the type of the cancer, or even the effect in animal models of a therapy on a cancer.

- 5 Cells also can be screened to determine whether such cells abnormally express the genes identified according to the invention.

The invention, in one aspect, is a method of diagnosing a disorder characterized by expression of a cancer associated antigen precursor coded for by a nucleic acid molecule. The method involves the steps of contacting a biological sample isolated from a subject with an agent that specifically binds to the nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof complexed with an MHC, preferably an HLA, molecule, wherein the nucleic acid molecule is a NA Group 1 nucleic acid molecule, and determining the interaction between the agent and the nucleic acid molecule, the expression product or fragment of the expression product as a determination of the disorder.

- 15 In one embodiment the agent is selected from the group consisting of (a) a nucleic acid molecule comprising NA Group 1 nucleic acid molecules or a fragment thereof, (b) a nucleic acid molecule comprising NA Group 3 nucleic acid molecules or a fragment thereof, (c) a nucleic acid molecule comprising NA Group 17 nucleic acid molecules or a fragment thereof, (d) an antibody that binds to an expression product, or a fragment thereof, of NA group 1 nucleic acids, (e) an antibody that binds to an expression product, or a fragment thereof, of NA group 3 nucleic acids, (f) an antibody that binds to an expression product, or a fragment thereof, of NA group 17 nucleic acids, (g) an agent that binds to a complex of an MHC, preferably HLA, molecule and a fragment of an expression product of a NA Group 1 nucleic acid, (h) an agent that binds to a complex of an MHC, preferably HLA, molecule and a fragment of an expression product of a NA group 3 nucleic acid, and (I) an agent that binds to a complex of an MHC, preferably HLA, molecule and a fragment of an expression product of a NA Group 17 nucleic acid.

The disorder may be characterized by expression of a plurality of cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which is specific for a different human cancer associated antigen precursor, and wherein said plurality of agents is at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9 or at least 10 such agents.

In each of the above embodiments the agent may be specific for a human cancer associated antigen precursor that is a breast, a gastric, a lung, a prostate, a renal or a colon cancer associated antigen precursor.

In another aspect the invention is a method for determining regression, progression or onset of a condition characterized by expression of abnormal levels of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule. The method involves the steps of monitoring a sample, from a subject who has or is suspected of having the condition, for a parameter selected from the group consisting of (i) the protein, (ii) a peptide derived from the protein, (iii) an antibody which selectively binds the protein or peptide, and (iv) cytolytic T cells specific for a complex of the peptide derived from the protein and an MHC molecule, as a determination of regression, progression or onset of said condition. In one embodiment the sample is a body fluid, a body effusion or a tissue.

In another embodiment the step of monitoring comprises contacting the sample with a detectable agent selected from the group consisting of (a) an antibody which selectively binds the protein of (i), or the peptide of (ii), (b) a protein or peptide which binds the antibody of (iii), and (c) a cell which presents the complex of the peptide and MHC molecule of (iv). In a preferred embodiment the antibody, the protein, the peptide or the cell is labeled with a radioactive label or an enzyme. The sample in a preferred embodiment is assayed for the peptide.

According to another embodiment the nucleic acid molecule is one of the following: a NA Group 3 molecule, a NA Group 11 molecule, a NA Group 12 molecule, a NA Group 13 molecule, a NA Group 14 molecule, a NA Group 15 molecule, or a NA Group 16 molecule. In yet another embodiment the protein is a plurality of proteins, the parameter is a plurality of parameters, each of the plurality of parameters being specific for a different of the plurality of proteins.

The invention in another aspect is a pharmaceutical preparation for a human subject. The pharmaceutical preparation includes an agent which when administered to the subject enriches selectively the presence of complexes of an HLA molecule and a human cancer associated antigen, and a pharmaceutically acceptable carrier, wherein the human cancer associated antigen is a fragment of a human cancer associated antigen precursor encoded by a nucleic acid molecule which comprises a NA Group 1 molecule. In one embodiment the nucleic acid molecule is a NA Group 3 nucleic acid molecule.



The agent in one embodiment comprises a plurality of agents, each of which enriches selectively in the subject complexes of an HLA molecule and a different human cancer associated antigen. Preferably the plurality is at least two, at least three, at least four or at least 5 different such agents.

5 In another embodiment the agent is selected from the group consisting of (1) an isolated polypeptide comprising the human cancer associated antigen, or a functional variant thereof, (2) an isolated nucleic acid operably linked to a promoter for expressing the isolated polypeptide, or functional variant thereof, (3) a host cell expressing the isolated polypeptide, or functional variant thereof, and (4) isolated complexes of the polypeptide, or functional  
10 variant thereof, and an HLA molecule.

The agent may be a cell expressing an isolated polypeptide. In one embodiment the agent is a cell expressing an isolated polypeptide comprising the human cancer associated antigen or a functional variant thereof, and wherein the cell is nonproliferative. In another embodiment the agent is a cell expressing an isolated polypeptide comprising the human cancer  
15 associated antigen or a functional variant thereof, and wherein the cell expresses an HLA molecule that binds the polypeptide. The cell can express one or both of the polypeptide and HLA molecule recombinantly. In another preferred embodiment the cell is nonproliferative. In yet another embodiment the agent is at least two, at least three, at least four or at least five different polypeptides, each representing a different human cancer associated antigen or  
20 functional variant thereof.

The agent in one embodiment is a PP Group 2 polypeptide. In other embodiments the agent is a PP Group 3 polypeptide or a PP Group 4 polypeptide.

In an embodiment each of the pharmaceutical preparations described herein also includes an adjuvant.

25 According to another aspect the invention, a composition is provided of an isolated agent that binds selectively a PP Group 1 polypeptide. In separate embodiments the agent binds selectively to a polypeptide selected from the following: a PP Group 3 polypeptide, a PP Group 11 polypeptide, a PP Group 12 polypeptide, a PP Group 13 polypeptide, a PP Group 14 polypeptide, a PP Group 15 polypeptide, and a PP Group 16 polypeptide. In other  
30 embodiments, the agent is a plurality of different agents that bind selectively at least two, at least three, at least four, or at least five different such polypeptides. In each of the above described embodiments the agent may be an antibody.

In another aspect the invention is a composition of matter .composed of a conjugate of the agent of the above-described compositions of the invention and a therapeutic or diagnostic agent. Preferably the conjugate is of the agent and a therapeutic or diagnostic that is an antineoplastic.

5 The invention in another aspect is a pharmaceutical composition of an isolated nucleic acid molecule selected from the group consisting of: (1) NA Group 1 molecules, and (2) NA Group 2 molecules, and a pharmaceutically acceptable carrier. In one embodiment the isolated nucleic acid molecule comprises a NA Group 3 or NA Group 4 molecule. In another embodiment the isolated nucleic acid molecule comprises at least two isolated nucleic acid  
10 molecules coding for two different polypeptides, each polypeptide comprising a different cancer associated antigen.

Preferably the pharmaceutical composition also includes an expression vector with a promoter operably linked to the isolated nucleic acid molecule. In another embodiment the pharmaceutical composition also includes a host cell recombinantly expressing the isolated  
15 nucleic acid molecule.

According to another aspect of the invention a pharmaceutical composition is provided. The pharmaceutical composition includes an isolated polypeptide comprising a PP Group 1 or a PP Group 2 polypeptide, and a pharmaceutically acceptable carrier. In one embodiment the isolated polypeptide comprises a PP Group 3 or a PP Group 4 polypeptide.

20 In another embodiment the isolated polypeptide comprises at least two different polypeptides, each comprising a different cancer associated antigen. In separate embodiments the isolated polypeptides are selected from the following: PP Group 11 polypeptides or HLA binding fragments thereof, PP Group 12 polypeptides or HLA binding fragments thereof, PP Group 13 polypeptides or HLA binding fragments thereof, PP Group 14 polypeptides or HLA  
25 binding fragments thereof, PP Group 15 polypeptides or HLA binding fragments thereof, or PP Group 16 polypeptides or HLA binding fragments thereof.

In an embodiment each of the pharmaceutical compositions described herein also includes an adjuvant.

Another aspect the invention is an isolated nucleic acid molecule comprising a NA  
30 Group 3 molecule. Another aspect the invention is an isolated nucleic acid molecule comprising a NA Group 4 molecule. In separate embodiments the isolated nucleic acid molecules are selected from the following: a Group 11 molecule or a functional fragment

thereof, a Group 12 molecule or a functional fragment thereof, a Group 13 molecule or a functional fragment thereof, a Group 14 molecule or a functional fragment thereof, a Group 15 molecule or a functional fragment thereof, or a Group 16 molecule or a functional fragment thereof.

5           The invention in another aspect is an isolated nucleic acid molecule selected from the group consisting of (a) a fragment of a nucleic acid selected from the group of nucleic acid molecules consisting of SEQ ID numbered below and comprising all nucleic acid sequences among SEQ ID NOs 1-816, of sufficient length to represent a sequence unique within the human genome, and identifying a nucleic acid encoding a human cancer associated antigen precursor, (b) complements of (a), provided that the fragment includes a sequence of  
10 contiguous nucleotides which is not identical to any sequence selected from the sequence group consisting of (1) sequences having the GenBank accession numbers of the sequence Group 1, (2) complements of (1), and (3) fragments of (1) and (2).

          In one embodiment the sequence of contiguous nucleotides is selected from the group  
15 consisting of: (1) at least two contiguous nucleotides nonidentical to the sequence Group 1, (2) at least three contiguous nucleotides nonidentical to the sequence Group 1, (3) at least four contiguous nucleotides nonidentical to the sequence Group 1, (4) at least five contiguous nucleotides nonidentical to the sequence Group 1, (5) at least six contiguous nucleotides nonidentical to the sequence Group 1, or (6) at least seven contiguous nucleotides nonidentical  
20 to the sequence Group 1.

          In another embodiment the fragment has a size selected from the group consisting of at least: 8 nucleotides, 10 nucleotides, 12 nucleotides, 14 nucleotides, 16 nucleotides, 18 nucleotides, 20, nucleotides, 22 nucleotides, 24 nucleotides, 26 nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides, 200 nucleotides, 1000 nucleotides  
25 and every integer length therebetween.

          In yet another embodiment the molecule encodes a polypeptide which, or a fragment of which, binds a human HLA receptor or a human antibody.

          Another aspect of the invention is an expression vector comprising an isolated nucleic acid molecule of the invention described above operably linked to a promoter.

30           According to one aspect the invention is an expression vector comprising a nucleic acid operably linked to a promoter, wherein the nucleic acid is a NA Group 2 molecule. In another aspect the invention is an expression vector comprising a NA Group 1 or Group 2 molecule

and a nucleic acid encoding an MHC, preferably HLA, molecule.

In yet another aspect the invention is a host cell transformed or transfected with an expression vector of the invention described above.

In another aspect the invention is a host cell transformed or transfected with an expression vector comprising an isolated nucleic acid molecule of the invention described above operably linked to a promoter, or an expression vector comprising a nucleic acid operably linked to a promoter, wherein the nucleic acid is a NA Group 1 or 2 molecule and further comprising a nucleic acid encoding HLA.

According to another aspect of the invention an isolated polypeptide encoded by the isolated nucleic acid molecules the invention, described above, is provided. These include PP Group 1-17 polypeptides. The invention also includes a fragment of the polypeptide which is immunogenic. In one embodiment the fragment, or a portion of the fragment, binds HLA or a human antibody.

The invention includes in another aspect an isolated fragment of a human cancer associated antigen precursor which, or portion of which, binds HLA or a human antibody, wherein the precursor is encoded by a nucleic acid molecule that is a NA Group 1 molecule. In one embodiment the fragment is part of a complex with HLA. In another embodiment the fragment is between 8 and 12 amino acids in length. In another embodiment the invention includes an isolated polypeptide comprising a fragment of the polypeptide of sufficient length to represent a sequence unique within the human genome and identifying a polypeptide that is a human cancer associated antigen precursor.

According to another aspect of the invention a kit for detecting the presence of the expression of a cancer associated antigen precursor is provided. The kit includes a pair of isolated nucleic acid molecules each of which consists essentially of a molecule selected from the group consisting of (a) a 12-32 nucleotide contiguous segment of the nucleotide sequence of any of the NA Group 1 molecules and (b) complements of ("a"), wherein the contiguous segments are nonoverlapping. In one embodiment the pair of isolated nucleic acid molecules is constructed and arranged to selectively amplify an isolated nucleic acid molecule that is a NA Group 3 molecule. Preferably, the pair amplifies a human NA Group 3 molecule.

According to another aspect of the invention a method for treating a subject with a disorder characterized by expression of a human cancer associated antigen precursor is provided. The method includes the step of administering to the subject an amount of an agent,

which enriches selectively in the subject the presence of complexes of an HLA molecule and a human cancer associated antigen, effective to ameliorate the disorder, wherein the human cancer associated antigen is a fragment of a human cancer associated antigen precursor encoded by a nucleic acid molecule selected from the group consisting of (a) a nucleic acid molecule comprising NA group 1 nucleic acid molecules, (b) a nucleic acid molecule comprising NA group 3 nucleic acid molecules, (c) a nucleic acid molecule comprising NA group 17 nucleic acid molecules.

In one embodiment the disorder is characterized by expression of a plurality of human cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which enriches selectively in the subject the presence of complexes of an HLA molecule and a different human cancer associated antigen. Preferably the plurality is at least 2, at least 3, at least 4, or at least 5 such agents.

In another embodiment the agent is an isolated polypeptide selected from the group consisting of PP Group 1, PP Group 2, PP Group 3, PP Group 4, PP Group 5, PP Group 6, PP Group 7, PP Group 8, PP Group 9, PP Group 10, PP Group 11, PP Group 12, PP Group 13, PP Group 14, PP Group 15, PP Group 16 and PP Group 17 polypeptides.

In yet another embodiment the disorder is cancer.

According to another aspect the invention is a method for treating a subject having a condition characterized by expression of a cancer associated antigen precursor in cells of the subject. The method includes the steps of (i) removing an immunoreactive cell containing sample from the subject, (ii) contacting the immunoreactive cell containing sample to the host cell under conditions favoring production of cytolytic T cells against a human cancer associated antigen which is a fragment of the precursor, (iii) introducing the cytolytic T cells to the subject in an amount effective to lyse cells which express the human cancer associated antigen, wherein the host cell is transformed or transfected with an expression vector comprising an isolated nucleic acid molecule operably linked to a promoter, the isolated nucleic acid molecule being selected from the group of nucleic acid molecules consisting of NA Group 1, NA Group 2, NA Group 3, NA Group 4, NA Group 5, NA Group 6, NA Group 7, NA Group 8, NA Group 9, NA Group 10, NA Group 11, NA Group 12, NA Group 13, NA Group 14, NA Group 15, NA Group 16, and NA Group 17.

In one embodiment the host cell recombinantly expresses an HLA molecule which binds the human cancer associated antigen. In another embodiment the host cell endogenously

expresses an HLA molecule which binds the human cancer associated antigen.

The invention includes in another aspect a method for treating a subject having a condition characterized by expression of a cancer associated antigen precursor in cells of the subject. The method includes the steps of (I) identifying a nucleic acid molecule expressed by the cells associated with said condition, wherein said nucleic acid molecule is a NA Group 1 molecule (ii) transfecting a host cell with a nucleic acid selected from the group consisting of (a) the nucleic acid molecule identified, (b) a fragment of the nucleic acid identified which includes a segment coding for a cancer associated antigen, (c) deletions, substitutions or additions to (a) or (b), and (d) degenerates of (a), (b), or (c); (iii) culturing said transfected host cells to express the transfected nucleic acid molecule, and; (iv) introducing an amount of said host cells or an extract thereof to the subject effective to increase an immune response against the cells of the subject associated with the condition. Preferably, the antigen is a human antigen and the subject is a human.

In one embodiment the method also includes the step of (a) identifying an MHC molecule which presents a portion of an expression product of the nucleic acid molecule, wherein the host cell expresses the same MHC molecule as identified in (a) and wherein the host cell presents an MHC binding portion of the expression product of the nucleic acid molecule.

In another embodiment the method also includes the step of treating the host cells to render them non-proliferative.

In yet another embodiment the immune response comprises a B-cell response or a T cell response. Preferably the response is a T-cell response which comprises generation of cytolytic T-cells specific for the host cells presenting the portion of the expression product of the nucleic acid molecule or cells of the subject expressing the human cancer associated antigen.

In another embodiment the nucleic acid molecule is a NA Group 3 molecule.

Another aspect of the invention is a method for treating or diagnosing or monitoring a subject having a condition characterized by expression of an abnormal amount of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule. The method includes the step of administering to the subject an antibody which specifically binds to the protein or a peptide derived therefrom, the antibody being coupled to a therapeutically useful agent, in an amount effective to treat the condition.

In one embodiment the antibody is a monoclonal antibody. Preferably the monoclonal antibody is a chimeric antibody or a humanized antibody.

In another aspect the invention is a method for treating a condition characterized by expression in a subject of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule. The method involves the step of administering to a subject at least one of the pharmaceutical compositions of the invention described above in an amount effective to prevent, delay the onset of, or inhibit the condition in the subject. In one embodiment the condition is cancer. In another embodiment the method includes the step of first identifying that the subject expresses in a tissue abnormal amounts of the protein.

The invention in another aspect is a method for treating a subject having a condition characterized by expression of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule. The method includes the steps of (i) identifying cells from the subject which express abnormal amounts of the protein; (ii) isolating a sample of the cells; (iii) cultivating the cells, and (iv) introducing the cells to the subject in an amount effective to provoke an immune response against the cells.

In one embodiment the cells express a protein selected from the group consisting of a PP Group 11 protein, a PP Group 12 protein, a PP Group 13 protein, PP Group 14 protein, a PP Group 15 protein and a PP Group 16 protein. In another embodiment the method includes the step of rendering the cells non-proliferative, prior to introducing them to the subject.

In another aspect the invention is a method for treating a pathological cell condition characterized by abnormal expression of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule. The method includes the step of administering to a subject in need thereof an effective amount of an agent which inhibits the expression or activity of the protein.

In one embodiment the agent is an inhibiting antibody which selectively binds to the protein and wherein the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody. In another embodiment the agent is an antisense nucleic acid molecule which selectively binds to the nucleic acid molecule which encodes the protein. In yet another important embodiment the nucleic acid molecule is a NA Group 3 nucleic acid molecule.

The invention includes in another aspect a composition of matter useful in stimulating an immune response to a plurality of a protein encoded by nucleic acid molecules that are NA Group 1 molecules. The composition is a plurality of peptides derived from the amino acid

sequences of the proteins, wherein the peptides bind to one or more MHC molecules presented on the surface of the cells which express an abnormal amount of the protein.

In one embodiment at least a portion of the plurality of peptides bind to MHC molecules and elicit a cytolytic response thereto. In another embodiment the composition of matter includes an adjuvant. In another embodiment the adjuvant is a saponin, GM-CSF, or an interleukin.

According to another aspect the invention is an isolated antibody which selectively binds to a complex of: (i) a peptide derived from a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule and (ii) an MHC molecule to which binds the peptide to form the complex, wherein the isolated antibody does not bind to (i) or (ii) alone.

In one embodiment the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody.

The invention also involves the use of the genes, gene products, fragments thereof, agents which bind thereto, and so on in the preparation of medicaments. A particular medicament is for treating cancer and a more particular medicament is for treating breast cancer, lung cancer, renal cancer, colon cancer, prostate cancer or gastric cancer.

### **Detailed Description of the Invention**

In the above summary and in the ensuing description, lists of sequences are provided.

The lists are meant to embrace each single sequence separately, two or more sequences together where they form a part of the same gene, any combination of two or more sequences which relate to different genes, including and up to the total number on the list, as if each and every combination were separately and specifically enumerated. Likewise, when mentioning fragment size, it is intended that a range embrace the smallest fragment mentioned to the full-length of the sequence (-1 so that it is a fragment), each and every fragment length intended as if specifically enumerated. Thus, if a fragment could be between 10 and 15 in length, it is explicitly meant to mean 10, 11, 12, 13, 14, or 15 in length.

The summary and the claims mention antigen precursors and antigens. As used in the summary and in the claims, a precursor is substantially the full-length protein encoded by the coding region of the isolated DNA and the antigen is a peptide which complexes with MHC, preferably HLA, and which participates in the immune response as part of that complex. Such antigens are typically 9 amino acids long, although this may vary slightly.



As used herein, a subject is a human, non-human primate, cow, horse, pig, sheep, goat, dog, cat or rodent. In all embodiments human cancer antigens and human subjects are preferred.

The present invention in one aspect involves the cloning of cDNAs encoding human cancer associated antigen precursors using autologous antisera of subjects having cancer. The sequences of the clones representing genes identified according to the methods described herein are presented in the attached Sequence Listing, and the predicted amino acid sequences of some clones also are presented. Of the foregoing, it can be seen that some of the clones are considered completely novel as no nucleotide or amino acid homologies to coding regions were found in the databases searched. Other clones are novel but have some homology to sequences deposited in databases (mainly EST sequences). Nevertheless, the entire gene sequence was not previously known. In some cases no function was suspected and in other cases, even if a function was suspected, it was not known that the gene was associated with cancer. In all cases, it was not known or suspected that the gene encoded a cancer antigen which reacted with antibody from autologous sera. Analysis of the clone sequences by comparison to nucleic acid and protein databases determined that still other of the clones surprisingly are closely related to other previously-cloned genes. The sequences of these related genes is also presented in the Sequence Listing. The nature of the foregoing genes as encoding antigens recognized by the immune systems of cancer patients is, of course, unexpected.

The invention thus involves in one aspect cancer associated antigen polypeptides, genes encoding those polypeptides, functional modifications and variants of the foregoing, useful fragments of the foregoing, as well as diagnostics and therapeutics relating thereto.

Homologs and alleles of the cancer associated antigen nucleic acids of the invention can be identified by conventional techniques. Thus, an aspect of the invention is those nucleic acid sequences which code for cancer associated antigen precursors. Because this application contains so many sequences, the following chart is provided to identify the various groups of sequences discussed in the claims and in the summary:

#### "Nucleic Acid Sequences"

30 NA Group 1. (a) nucleic acid molecules which hybridize under stringent conditions to a molecule consisting of a nucleic acid sequence selected from the group consisting of nucleic acid sequences among SEQ ID NOs 1-816 and which code for a cancer associated antigen precursor,

(b) deletions, additions and substitutions which code for a respective cancer associated antigen precursor,

(c) nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code, and

5 (d) complements of (a), (b) or (c).

NA Group 2. Fragments of NA Group 1, which codes for a polypeptide which, or a portion of which, binds an MHC molecule to form a complex recognized by a an autologous antibody or lymphocyte.

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NA Group 3. The subset of NA Group 1 where the nucleotide sequence is selected from the group consisting of:

(a) previously unknown human nucleic acids coding for a human cancer associated antigen precursor,

15 (b) deletions, additions and substitutions which code for a respective human cancer associated antigen precursor,

(c) nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code, and

(d) complements of (a), (b) or (c).

20 NA Group 4. Fragments of NA Group 3, which code for a polypeptide which, or a portion of which, binds to an MHC molecule to form a complex recognized by an autologous antibody or lymphocyte.

NA Group 5. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human breast cancer associated antigen precursor.

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NA Group 6. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human colon cancer associated antigen precursor.

30 NA Group 7. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human gastric cancer associated antigen precursor.

NA Group 8. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human lung cancer associated antigen precursor.

NA Group 9. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human renal cancer associated antigen precursor.

NA Group 10. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human prostate cancer associated antigen precursor.

NA Group 11. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human breast cancer associated antigen precursor.

NA Group 12. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human colon cancer associated antigen precursor.

NA Group 13. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human gastric cancer associated antigen precursor.

NA Group 14. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human lung cancer associated antigen precursor.

NA Group 15. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human renal cancer associated antigen precursor.

NA Group 16. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human prostate cancer associated antigen precursor.

NA Group 17. A subset of NA Group 1, comprising human cancer associated antigens that react with allogenic cancer antisera.

#### Polypeptide Sequences

PP Group 1. Polypeptides encoded by NA Group 1.

- PP Group 2. Polypeptides encoded by NA Group 2  
PP Group 3. Polypeptides encoded by NA Group 3.  
PP Group 4. Polypeptides encoded by NA Group 4.  
PP Group 5. Polypeptides encoded by NA Group 5.  
5 PP Group 6. Polypeptides encoded by NA Group 6.  
PP Group 7. Polypeptides encoded by NA Group 7.  
PP Group 8. Polypeptides encoded by NA Group 8.  
PP Group 9. Polypeptides encoded by NA Group 9.  
PP Group 10. Polypeptides encoded by NA Group 10.  
10 PP Group 11. Polypeptides encoded by NA Group 11.  
PP Group 12. Polypeptides encoded by NA Group 12.  
PP Group 13. Polypeptides encoded by NA Group 13.  
PP Group 14. Polypeptides encoded by NA Group 14.  
PP Group 15. Polypeptides encoded by NA Group 15.  
15 PP Group 16. Polypeptides encoded by NA Group 16.  
PP Group 17. Polypeptides encoded by NA Group 17.

The term "stringent conditions" as used herein refers to parameters with which the art is familiar. Nucleic acid hybridization parameters may be found in references which compile such methods, e.g. *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1989, or *Current Protocols in Molecular Biology*, F.M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York. More specifically, stringent conditions, as used herein, refers, for example, to hybridization at 65°C in hybridization buffer (3.5 x SSC, 0.02% Ficoll, 0.02% polyvinyl pyrrolidone, 0.02% Bovine Serum Albumin, 2.5mM NaH<sub>2</sub>PO<sub>4</sub>(pH7), 0.5% SDS, 2mM EDTA). SSC is 0.15M sodium chloride/0.15M sodium citrate, pH7; SDS is sodium dodecyl sulphate; and EDTA is ethylenediaminetetracetic acid. After hybridization, the membrane upon which the DNA is transferred is washed, for example, in 2 x SSC at room temperature and then at 0.1 - 0.5 x SSC/0.1 x SDS at temperatures up to 68°C.

30 There are other conditions, reagents, and so forth which can be used, which result in a similar degree of stringency. The skilled artisan will be familiar with such conditions, and thus they are not given here. It will be understood, however, that the skilled artisan will be able to

manipulate the conditions in a manner to permit the clear identification of homologs and alleles of cancer associated antigen nucleic acids of the invention (e.g., by using lower stringency conditions). The skilled artisan also is familiar with the methodology for screening cells and libraries for expression of such molecules which then are routinely isolated, followed by  
5 isolation of the pertinent nucleic acid molecule and sequencing.

In general homologs and alleles typically will share at least 40% nucleotide identity and/or at least 50% amino acid identity to the sequences of breast cancer associated antigen nucleic acid and polypeptides, respectively, in some instances will share at least 50% nucleotide identity and/or at least 65% amino acid identity and in still other instances will share at least 60%  
10 nucleotide identity and/or at least 75% amino acid identity. The homology can be calculated using various, publicly available software tools developed by NCBI (Bethesda, Maryland) that can be obtained through the internet (<ftp://ncbi.nlm.nih.gov/pub/>). Exemplary tools include the BLAST system available at <http://www.ncbi.nlm.nih.gov>. Pairwise and ClustalW alignments (BLOSUM30 matrix setting) as well as Kyte-Doolittle hydropathic analysis can be obtained  
15 using the MacVetor sequence analysis software (Oxford Molecular Group). Watson-Crick complements of the foregoing nucleic acids also are embraced by the invention.

In screening for cancer associated antigen genes, a Southern blot may be performed using the foregoing conditions, together with a radioactive probe. After washing the membrane to which the DNA is finally transferred, the membrane can be placed against X-ray film to detect  
20 the radioactive signal. In screening for the expression of cancer associated antigen nucleic acids, Northern blot hybridizations using the foregoing conditions (see also the Examples) can be performed on samples taken from breast cancer patients or subjects suspected of having a condition characterized by expression of breast cancer associated antigen genes. Amplification protocols such as polymerase chain reaction using primers which hybridize to the sequences  
25 presented also can be used for detection of the cancer associated antigen genes or expression thereof.

The breast cancer associated genes correspond to SEQ ID NOs. 1-40 and 66. The preferred breast cancer associated antigens for the methods of diagnosis disclosed herein are those set forth in SEQ ID NOs:[31, 33 and 34], which were found to react with allogeneic breast  
30 cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The colon cancer associated genes correspond to SEQ ID Nos. 544-586, even numbers

only. The preferred colon cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic colon cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The gastric cancer associated genes correspond to SEQ ID NOs 176-436 and 588-674.

- 5 The preferred gastric cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic gastric cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

- 10 The renal cancer associated genes correspond to SEQ ID Nos. 89-169, odd numbers only, and 170, 172, and 174. The preferred renal cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic renal cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

- 15 The lung cancer associated genes correspond to SEQ ID Nos. 689, 691, 692, 694, 696-707, 709, 711, and 712. The preferred lung cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic lung cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

- 20 The prostate cancer associated genes correspond to SEQ ID NOs 437-543. The preferred prostate cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic prostate cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

- 25 The invention also includes degenerate nucleic acids which include alternative codons to those present in the native materials. For example, serine residues are encoded by the codons TCA, AGT, TCC, TCG, TCT and AGC. Each of the six codons is equivalent for the purposes of encoding a serine residue. Thus, it will be apparent to one of ordinary skill in the art that any of the serine-encoding nucleotide triplets may be employed to direct the protein synthesis apparatus, *in vitro* or *in vivo*, to incorporate a serine residue into an elongating breast cancer associated antigen polypeptide. Similarly, nucleotide sequence triplets which encode other amino acid residues include, but are not limited to: CCA, CCC, CCG and CCT (proline codons); CGA, CGC, CGG, CGT, AGA and AGG (arginine codons); ACA, ACC, ACG and ACT (threonine codons); AAC and AAT (asparagine codons); and ATA, ATC and ATT (isoleucine codons).  
30 Other amino acid residues may be encoded similarly by multiple nucleotide sequences. Thus,

the invention embraces degenerate nucleic acids that differ from the biologically isolated nucleic acids in codon sequence due to the degeneracy of the genetic code.

The invention also provides isolated unique fragments of cancer associated antigen nucleic acid sequences or complements thereof. A unique fragment is one that is a 'signature' for the larger nucleic acid. It, for example, is long enough to assure that its precise sequence is not found in molecules within the human genome outside of the cancer associated antigen nucleic acids defined above (and human alleles). Those of ordinary skill in the art may apply no more than routine procedures to determine if a fragment is unique within the human genome. Unique fragments, however, exclude fragments completely composed of the nucleotide sequences of any of GenBank accession numbers listed in Table 1 or other previously published sequences as of the filing date of the priority documents for sequences listed in a respective priority document or the filing date of this application for sequences listed for the first time in this application which overlap the sequences of the invention.

A fragment which is completely composed of the sequence described in the foregoing GenBank deposits is one which does not include any of the nucleotides unique to the sequences of the invention. Thus, a unique fragment must contain a nucleotide sequence other than the exact sequence of those in GenBank or fragments thereof. The difference may be an addition, deletion or substitution with respect to the GenBank sequence or it may be a sequence wholly separate from the GenBank sequence.

Unique fragments can be used as probes in Southern and Northern blot assays to identify such nucleic acids, or can be used in amplification assays such as those employing PCR. As known to those skilled in the art, large probes such as 200, 250, 300 or more nucleotides are preferred for certain uses such as Southern and Northern blots, while smaller fragments will be preferred for uses such as PCR. Unique fragments also can be used to produce fusion proteins for generating antibodies or determining binding of the polypeptide fragments, or for generating immunoassay components. Likewise, unique fragments can be employed to produce nonfused fragments of the cancer associated antigen polypeptides, useful, for example, in the preparation of antibodies, and in immunoassays. Unique fragments further can be used as antisense molecules to inhibit the expression of cancer associated antigen nucleic acids and polypeptides, particularly for therapeutic purposes as described in greater detail below.

As will be recognized by those skilled in the art, the size of the unique fragment will depend upon its conservancy in the genetic code. Thus, some regions of cancer associated antigen sequences and complements thereof will require longer segments to be unique while others will require only short segments, typically between 12 and 32 nucleotides (e.g. 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31 and 32 or more bases long, up to the entire length of the disclosed sequence. As mentioned above, this disclosure intends to embrace each and every fragment of each sequence, beginning at the first nucleotide, the second nucleotide and so on, up to 8 nucleotides short of the end, and ending anywhere from nucleotide number 8, 9, 10 and so on for each sequence, up to the very last nucleotide, (provided the sequence is unique as described above).

Virtually any segment of the polypeptide coding region of novel cancer associated antigen nucleic acids, or complements thereof, that is 18 or more nucleotides in length will be unique. Those skilled in the art are well versed in methods for selecting such sequences, typically on the basis of the ability of the unique fragment to selectively distinguish the sequence of interest from other sequences in the human genome of the fragment to those on known databases typically is all that is necessary, although *in vitro* confirmatory hybridization and sequencing analysis may be performed. Especially preferred include nucleic acids encoding a series of epitopes, known as "polytopes". The epitopes can be arranged in sequential or overlapping fashion (*see, e.g.,* Thomson et al., *Proc. Natl. Acad. Sci. USA* 92:5845-5849, 1995; Gilbert et al., *Nature Biotechnol.* 15:1280-1284, 1997), with or without the natural flanking sequences, and can be separated by unrelated linker sequences if desired. The polytope is processed to generated individual epitopes which are recognized by the immune system for generation of immune responses.

Thus, for example, peptides derived from a polypeptide having an amino acid sequence encoded by one of the nucleic acid disclosed herein, and which are presented by MHC molecules and recognized by CTL or T helper lymphocytes, can be combined with peptides from one or more other cancer associated antigens (e.g. by preparation of hybrid nucleic acids or polypeptides) to form "polytopes". The two or more peptides (or nucleic acids encoding the peptides) can be selected from those described herein, or they can include one or more peptides of previously known cancer associated antigens. Exemplary cancer associated peptide antigens that can be administered to induce or enhance an immune response are derived from tumor associated genes and encoded proteins including MAGE-1, MAGE-2, MAGE-3, MAGE-4, MAGE-5, MAGE-6, MAGE-7,



MAGE-8, MAGE-9, MAGE-10, MAGE-11, GAGE-1, GAGE-2, GAGE-3, GAGE-4, GAGE-5, GAGE-6, BAGE-1, RAGE-1, LB33/MUM-1, PRAME, NAG, MAGE-Xp2, MAGE-Xp3, MAGE-Xp4, tyrosinase, brain glycogen phosphorylase, Melan-A, and MAGE-C1. See, for example, PCT application publication no. WO96/10577. Other examples will be known to one of ordinary skill in the art (for example, see Coulie, *Stem Cells* 13:393-403, 1995), and can be used in the invention in a like manner as those disclosed herein. One of ordinary skill in the art can prepare polypeptides comprising one or more peptides and one or more of the foregoing cancer associated peptides, or nucleic acids encoding such polypeptides, according to standard procedures of molecular biology.

Thus polytopes are groups of two or more potentially immunogenic or immune response stimulating peptides which can be joined together in various arrangements (e.g. concatenated, overlapping). The polytope (or nucleic acid encoding the polytope) can be administered in a standard immunization protocol, e.g. to animals, to test the effectiveness of the polytope in stimulating, enhancing and/or provoking an immune response.

The peptides can be joined together directly or via the use of flanking sequences to form polytopes, and the use of polytopes as vaccines is well known in the art (see, e.g., Thomson et al., *Proc. Acad. Natl. Acad. Sci USA* 92(13):5845-5849, 1995; Gilbert et al., *Nature Biotechnol.* 15(12):1280-1284, 1997; Thomson et al., *J. Immunol.* 157(2):822-826, 1996; Tam et al., *J. Exp. Med.* 171(1):299-306, 1990).for example, Tam showed that polytopes consisting of both MHC class I and class II binding epitopes successfully generated antibody and protective immunity in a mouse model. Tam also demonstrated that polytopes comprising "strings" of epitopes are processed to yield individual epitopes which are presented by MHC molecules and recognized by CTLs. Thus polytopes containing various numbers and combinations of epitopes can be prepared and tested for recognition by CTLs and for efficacy in increasing an immune response.

It is known that tumors express a set of tumor antigens, of which only certain subsets may be expressed in the tumor of any given patient (for examples of this, see the Examples below). Polytopes can be prepared which correspond to the different combination of epitopes representing the subset of tumor rejection antigens expressed in a particular patient. Polytopes also can be prepared to reflect a broader spectrum of tumor rejection antigens known to be expressed by a tumor type. Polytopes can be introduced to a patient in need of such treatment as polypeptide structures, or via the use of nucleic acid delivery systems known in the art (see, e.g., Allsopp et al., *Eur. J.*

*Immunol.* 26(8):1951-1959, 1996). Adenovirus, pox virus, Ty-virus like particles, adeno-associated virus, plasmids, bacteria, etc. can be used in such delivery. One can test the polytope delivery systems in mouse models to determine efficacy of the delivery system. The systems also can be tested in human clinical trials.

5 In instances in which a human HLA class I molecule presents tumor rejection antigens derived from cancer associated nucleic acids, the expression vector may also include a nucleic acid sequence coding for the HLA molecule that presents any particular tumor rejection antigen derived from these nucleic acids and polypeptides. Alternatively, the nucleic acid sequence coding for such a HLA molecule can be contained within a separate expression vector. In a situation where the  
10 vector contains both coding sequences, the single vector can be used to transfect a cell which does not normally express either one. Where the coding sequences for a cancer associated antigen precursor and the HLA molecule which presents it are contained on separate expression vectors, the expression vectors can be cotransfected. The cancer associated antigen precursor coding sequence may be used alone, when, e.g. the host cell already expresses a HLA molecule which presents a  
15 cancer associated antigen derived from precursor molecules. Of course, there is no limit on the particular host cell which can be used. As the vectors which contain the two coding sequences may be used in any antigen-presenting cells if desired, and the gene for cancer associated antigen precursor can be used in host cells which do not express a HLA molecule which presents a cancer associated antigen. Further, cell-free transcription systems may be used in lieu of cells.

20 As mentioned above, the invention embraces antisense oligonucleotides that selectively bind to a nucleic acid molecule encoding a cancer associated antigen polypeptide, to reduce the expression of cancer associated antigens. This is desirable in virtually any medical condition wherein a reduction of expression of cancer associated antigens is desirable, e.g., in the treatment of cancer. This is also useful for *in vitro* or *in vivo* testing of the effects of a reduction of expression of  
25 one or more cancer associated antigens.

As used herein, the term "antisense oligonucleotide" or "antisense" describes an oligonucleotide that is an oligoribonucleotide, oligodeoxyribonucleotide, modified oligoribonucleotide, or modified oligodeoxyribonucleotide which hybridizes under physiological conditions to DNA comprising a particular gene or to an mRNA transcript of that gene and, thereby,  
30 inhibits the transcription of that gene and/or the translation of that mRNA. The antisense molecules

are designed so as to interfere with transcription or translation of a target gene upon hybridization with the target gene or transcript. Those skilled in the art will recognize that the exact length of the antisense oligonucleotide and its degree of complementarity with its target will depend upon the specific target selected, including the sequence of the target and the particular bases which comprise that sequence. It is preferred that the antisense oligonucleotide be constructed and arranged so as to bind selectively with the target under physiological conditions, i.e., to hybridize substantially more to the target sequence than to any other sequence in the target cell under physiological conditions. Based upon the sequences of nucleic acids encoding breast cancer associated antigen, or upon allelic or homologous genomic and/or cDNA sequences, one of skill in the art can easily choose and synthesize any of a number of appropriate antisense molecules for use in accordance with the present invention. In order to be sufficiently selective and potent for inhibition, such antisense oligonucleotides should comprise at least 10 and, more preferably, at least 15 consecutive bases which are complementary to the target, although in certain cases modified oligonucleotides as short as 7 bases in length have been used successfully as antisense oligonucleotides (Wagner et al., *Nature Biotechnol.* 14:840-844, 1996). Most preferably, the antisense oligonucleotides comprise a complementary sequence of 20-30 bases. Although oligonucleotides may be chosen which are antisense to any region of the gene or mRNA transcripts, in preferred embodiments the antisense oligonucleotides correspond to N-terminal or 5' upstream sites such as translation initiation, transcription initiation or promoter sites. In addition, 3'-untranslated regions may be targeted. Targeting to mRNA splicing sites has also been used in the art but may be less preferred if alternative mRNA splicing occurs. In addition, the antisense is targeted, preferably, to sites in which mRNA secondary structure is not expected (see, e.g., Sainio et al., *Cell Mol. Neurobiol.* 14(5):439-457, 1994) and at which proteins are not expected to bind. Finally, although the listed sequences are cDNA sequences, one of ordinary skill in the art may easily derive the genomic DNA corresponding to the cDNA of a cancer associated antigen. Thus, the present invention also provides for antisense oligonucleotides which are complementary to the genomic DNA corresponding to nucleic acids encoding breast cancer associated antigens. Similarly, antisense to allelic or homologous cDNAs and genomic DNAs are enabled without undue experimentation.

In one set of embodiments, the antisense oligonucleotides of the invention may be composed of "natural" deoxyribonucleotides, ribonucleotides, or any combination thereof. That is, the 5' end

of one native nucleotide and the 3' end of another native nucleotide may be covalently linked, as in natural systems, via a phosphodiester internucleoside linkage. These oligonucleotides may be prepared by art recognized methods which may be carried out manually or by an automated synthesizer. They also may be produced recombinantly by vectors.

5 In preferred embodiments, however, the antisense oligonucleotides of the invention also may include "modified" oligonucleotides. That is, the oligonucleotides may be modified in a number of ways which do not prevent them from hybridizing to their target but which enhance their stability or targeting or which otherwise enhance their therapeutic effectiveness.

The term "modified oligonucleotide" as used herein describes an oligonucleotide in which  
10 (1) at least two of its nucleotides are covalently linked via a synthetic internucleoside linkage (i.e., a linkage other than a phosphodiester linkage between the 5' end of one nucleotide and the 3' end of another nucleotide) and/or (2) a chemical group not normally associated with nucleic acids has been covalently attached to the oligonucleotide. Preferred synthetic internucleoside linkages are  
15 phosphorothioates, alkylphosphonates, phosphorodithioates, phosphate esters, alkylphosphonothioates, phosphoramidates, carbamates, carbonates, phosphate triesters, acetamides, carboxymethyl esters and peptides.

The term "modified oligonucleotide" also encompasses oligonucleotides with a covalently modified base and/or sugar. For example, modified oligonucleotides include oligonucleotides having backbone sugars which are covalently attached to low molecular weight organic groups other  
20 than a hydroxyl group at the 3' position and other than a phosphate group at the 5' position. Thus modified oligonucleotides may include a 2'-O-alkylated ribose group. In addition, modified oligonucleotides may include sugars such as arabinose instead of ribose. The present invention, thus, contemplates pharmaceutical preparations containing modified antisense molecules that are complementary to and hybridizable with, under physiological conditions, nucleic acids encoding  
25 breast cancer associated antigen polypeptides, together with pharmaceutically acceptable carriers.

Antisense oligonucleotides may be administered as part of a pharmaceutical composition. Such a pharmaceutical composition may include the antisense oligonucleotides in combination with any standard physiologically and/or pharmaceutically acceptable carriers which are known in the art. The compositions should be sterile and contain a therapeutically effective amount of the antisense  
30 oligonucleotides in a unit of weight or volume suitable for administration to a patient. The term

“pharmaceutically acceptable” means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredients. The term “physiologically acceptable” refers to a non-toxic material that is compatible with a biological system such as a cell, cell culture, tissue, or organism. The characteristics of the carrier will depend on the route of administration. Physiologically and pharmaceutically acceptable carriers include diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials which are well known in the art, as further described below.

As used herein, a “vector” may be any of a number of nucleic acids into which a desired sequence may be inserted by restriction and ligation for transport between different genetic environments or for expression in a host cell. Vectors are typically composed of DNA although RNA vectors are also available. Vectors include, but are not limited to, plasmids, phagemids and virus genomes. A cloning vector is one which is able to replicate in a host cell, and which is further characterized by one or more endonuclease restriction sites at which the vector may be cut in a determinable fashion and into which a desired DNA sequence may be ligated such that the new recombinant vector retains its ability to replicate in the host cell. In the case of plasmids, replication of the desired sequence may occur many times as the plasmid increases in copy number within the host bacterium or just a single time per host before the host reproduces by mitosis. In the case of phage, replication may occur actively during a lytic phase or passively during a lysogenic phase. An expression vector is one into which a desired DNA sequence may be inserted by restriction and ligation such that it is operably joined to regulatory sequences and may be expressed as an RNA transcript. Vectors may further contain one or more marker sequences suitable for use in the identification of cells which have or have not been transformed or transfected with the vector. Markers include, for example, genes encoding proteins which increase or decrease either resistance or sensitivity to antibiotics or other compounds, genes which encode enzymes whose activities are detectable by standard assays known in the art (e.g.,  $\beta$ -galactosidase or alkaline phosphatase), and genes which visibly affect the phenotype of transformed or transfected cells, hosts, colonies or plaques (e.g., green fluorescent protein). Preferred vectors are those capable of autonomous replication and expression of the structural gene products present in the DNA segments to which they are operably joined.

As used herein, a coding sequence and regulatory sequences are said to be “operably” joined

when they are covalently linked in such a way as to place the expression or transcription of the coding sequence under the influence or control of the regulatory sequences. If it is desired that the coding sequences be translated into a functional protein, two DNA sequences are said to be operably joined if induction of a promoter in the 5' regulatory sequences results in the transcription of the coding sequence and if the nature of the linkage between the two DNA sequences does not (1) result in the introduction of a frame-shift mutation, (2) interfere with the ability of the promoter region to direct the transcription of the coding sequences, or (3) interfere with the ability of the corresponding RNA transcript to be translated into a protein. Thus, a promoter region would be operably joined to a coding sequence if the promoter region were capable of effecting transcription of that DNA sequence such that the resulting transcript might be translated into the desired protein or polypeptide.

The precise nature of the regulatory sequences needed for gene expression may vary between species or cell types, but shall in general include, as necessary, 5' non-transcribed and 5' non-translated sequences involved with the initiation of transcription and translation respectively, such as a TATA box, capping sequence, CAAT sequence, and the like. Especially, such 5' non-transcribed regulatory sequences will include a promoter region which includes a promoter sequence for transcriptional control of the operably joined gene. Regulatory sequences may also include enhancer sequences or upstream activator sequences as desired. The vectors of the invention may optionally include 5' leader or signal sequences. The choice and design of an appropriate vector is within the ability and discretion of one of ordinary skill in the art.

Expression vectors containing all the necessary elements for expression are commercially available and known to those skilled in the art. See, e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Second Edition, Cold Spring Harbor Laboratory Press, 1989. Cells are genetically engineered by the introduction into the cells of heterologous DNA (RNA) encoding a breast cancer associated antigen polypeptide or fragment or variant thereof. That heterologous DNA (RNA) is placed under operable control of transcriptional elements to permit the expression of the heterologous DNA in the host cell.

Preferred systems for mRNA expression in mammalian cells are those such as pRc/CMV (available from Invitrogen, Carlsbad, CA) that contain a selectable marker such as a gene that confers G418 resistance (which facilitates the selection of stably transfected cell lines) and the

human cytomegalovirus (CMV) enhancer-promoter sequences. Additionally, suitable for expression in primate or canine cell lines is the pCEP4 vector (Invitrogen), which contains an Epstein Barr Virus (EBV) origin of replication, facilitating the maintenance of plasmid as a multicopy extrachromosomal element. Another expression vector is the pEF-BOS plasmid containing the promoter of polypeptide Elongation Factor 1 $\alpha$ , which stimulates efficiently transcription *in vitro*. The plasmid is described by Mishizuma and Nagata (*Nuc. Acids Res.* 18:5322, 1990), and its use in transfection experiments is disclosed by, for example, Demoulin (*Mol. Cell. Biol.* 16:4710-4716, 1996). Still another preferred expression vector is an adenovirus, described by Stratford-Perricaudet, which is defective for E1 and E3 proteins (*J. Clin. Invest.* 90:626-630, 1992). The use of the adenovirus as an Adeno.P1A recombinant for the expression of an antigen is disclosed by Warnier et al., in intradermal injection in mice for immunization against P1A (*Int. J. Cancer*, 67:303-310, 1996). Additional vectors for delivery of nucleic acid are provided below.

The invention also embraces so-called expression kits, which allow the artisan to prepare a desired expression vector or vectors. Such expression kits include at least separate portions of a vector and one or more of the previously discussed breast cancer associated antigen nucleic acid molecules. Other components may be added, as desired, as long as the previously mentioned nucleic acid molecules, which are required, are included. The invention also includes kits for amplification of a breast cancer associated antigen nucleic acid, including at least one pair of amplification primers which hybridize to a breast cancer associated antigen nucleic acid. The primers preferably are 12-32 nucleotides in length and are non-overlapping to prevent formation of "primer-dimers". One of the primers will hybridize to one strand of the breast cancer associated antigen nucleic acid and the second primer will hybridize to the complementary strand of the breast cancer associated antigen nucleic acid, in an arrangement which permits amplification of the breast cancer associated antigen nucleic acid. Selection of appropriate primer pairs is standard in the art. For example, the selection can be made with assistance of a computer program designed for such a purpose, optionally followed by testing the primers for amplification specificity and efficiency.

The invention also permits the construction of cancer associated antigen gene "knock-outs" in cells and in animals, providing materials for studying certain aspects of cancer and immune system responses to cancer.

The invention also provides isolated polypeptides (including whole proteins and partial

proteins) encoded by the foregoing cancer associated antigen nucleic acids. Such polypeptides are useful, for example, alone or as fusion proteins to generate antibodies, as components of an immunoassay or diagnostic assay or as therapeutics. Cancer associated antigen polypeptides can be isolated from biological samples including tissue or cell homogenates, and can also be expressed  
5 recombinantly in a variety of prokaryotic and eukaryotic expression systems by constructing an expression vector appropriate to the expression system, introducing the expression vector into the expression system, and isolating the recombinantly expressed protein. Short polypeptides, including antigenic peptides (such as are presented by MHC molecules on the surface of a cell for immune recognition) also can be synthesized chemically using well-established methods of peptide synthesis.

10 A unique fragment of a cancer associated antigen polypeptide, in general, has the features and characteristics of unique fragments as discussed above in connection with nucleic acids. As will be recognized by those skilled in the art, the size of the unique fragment will depend upon factors such as whether the fragment constitutes a portion of a conserved protein domain. Thus, some regions of breast cancer associated antigens will require longer segments to be unique while others  
15 will require only short segments, typically between 5 and 12 amino acids (e.g. 5, 6, 7, 8, 9, 10, 11 or 12 or more, including each integer up to the full length, amino acids long).

20 Unique fragments of a polypeptide preferably are those fragments which retain a distinct functional capability of the polypeptide. Functional capabilities which can be retained in a unique fragment of a polypeptide include interaction with antibodies, interaction with other polypeptides or fragments thereof, selective binding of nucleic acids or proteins, and enzymatic activity. One important activity is the ability to act as a signature for identifying the polypeptide. Another is the ability to complex with HLA and to provoke in a human an immune response. Those skilled in the art are well versed in methods for selecting unique amino acid sequences, typically on the basis of  
25 the ability of the unique fragment to selectively distinguish the sequence of interest from non-family members. A comparison of the sequence of the fragment to those on known databases typically is all that is necessary.

The invention embraces variants of the cancer associated antigen polypeptides described above. As used herein, a "variant" of a cancer associated antigen polypeptide is a polypeptide which contains one or more modifications to the primary amino acid sequence of a cancer associated  
30 antigen polypeptide. Modifications which create a cancer associated antigen variant can be made to



a cancer associated antigen polypeptide 1) to reduce or eliminate an activity of a cancer associated antigen polypeptide; 2) to enhance a property of a cancer associated antigen polypeptide, such as protein stability in an expression system or the stability of protein-protein binding; 3) to provide a novel activity or property to a cancer associated antigen polypeptide, such as addition of an antigenic epitope or addition of a detectable moiety; or 4) to provide equivalent or better binding to an HLA molecule. Modifications to a cancer associated antigen polypeptide are typically made to the nucleic acid which encodes the cancer associated antigen polypeptide, and can include deletions, point mutations, truncations, amino acid substitutions and additions of amino acids or non-amino acid moieties. Alternatively, modifications can be made directly to the polypeptide, such as by cleavage, addition of a linker molecule, addition of a detectable moiety, such as biotin, addition of a fatty acid, and the like. Modifications also embrace fusion proteins comprising all or part of the cancer associated antigen amino acid sequence. One of skill in the art will be familiar with methods for predicting the effect on protein conformation of a change in protein sequence, and can thus "design" a variant cancer associated antigen polypeptide according to known methods. One example of such a method is described by Dahiyat and Mayo in *Science* 278:82-87, 1997, whereby proteins can be designed *de novo*. The method can be applied to a known protein to vary a only a portion of the polypeptide sequence. By applying the computational methods of Dahiyat and Mayo, specific variants of a cancer associated antigen polypeptide can be proposed and tested to determine whether the variant retains a desired conformation.

In general, variants include cancer associated antigen polypeptides which are modified specifically to alter a feature of the polypeptide unrelated to its desired physiological activity. For example, cysteine residues can be substituted or deleted to prevent unwanted disulfide linkages. Similarly, certain amino acids can be changed to enhance expression of a breast cancer associated antigen polypeptide by eliminating proteolysis by proteases in an expression system (e.g., dibasic amino acid residues in yeast expression systems in which KEX2 protease activity is present).

Mutations of a nucleic acid which encode a cancer associated antigen polypeptide preferably preserve the amino acid reading frame of the coding sequence, and preferably do not create regions in the nucleic acid which are likely to hybridize to form secondary structures, such a hairpins or loops, which can be deleterious to expression of the variant polypeptide.

Mutations can be made by selecting an amino acid substitution, or by random mutagenesis of

a selected site in a nucleic acid which encodes the polypeptide. Variant polypeptides are then expressed and tested for one or more activities to determine which mutation provides a variant polypeptide with the desired properties. Further mutations can be made to variants (or to non-variant cancer associated antigen polypeptides) which are silent as to the amino acid sequence of the polypeptide, but which provide preferred codons for translation in a particular host. The preferred codons for translation of a nucleic acid in, e.g., *E. coli*, are well known to those of ordinary skill in the art. Still other mutations can be made to the noncoding sequences of a cancer associated antigen gene or cDNA clone to enhance expression of the polypeptide. The activity of variants of cancer associated antigen polypeptides can be tested by cloning the gene encoding the variant cancer associated antigen polypeptide into a bacterial or mammalian expression vector, introducing the vector into an appropriate host cell, expressing the variant cancer associated antigen polypeptide, and testing for a functional capability of the cancer associated antigen polypeptides as disclosed herein. For example, the variant cancer associated antigen polypeptide can be tested for reaction with autologous or allogeneic sera as disclosed in the Examples. Preparation of other variant polypeptides may favor testing of other activities, as will be known to one of ordinary skill in the art.

The skilled artisan will also realize that conservative amino acid substitutions may be made in cancer associated antigen polypeptides to provide functionally equivalent variants of the foregoing polypeptides, i.e., the variants retain the functional capabilities of the cancer associated antigen polypeptides. As used herein, a "conservative amino acid substitution" refers to an amino acid substitution which does not alter the relative charge or size characteristics of the protein in which the amino acid substitution is made. Variants can be prepared according to methods for altering polypeptide sequence known to one of ordinary skill in the art such as are found in references which compile such methods, e.g. *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1989, or *Current Protocols in Molecular Biology*, F.M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York. Exemplary functionally equivalent variants of the cancer associated antigen polypeptides include conservative amino acid substitutions of in the amino acid sequences of SEQ ID proteins disclosed herein. Conservative substitutions of amino acids include substitutions made amongst amino acids within the following groups: (a) M, I, L, V; (b) F, Y, W; (c) K, R, H; (d) A, G; (e) S, T; (f) Q, N; and (g) E, D.

For example, upon determining that a peptide derived from a cancer associated antigen polypeptide is presented by an MHC molecule and recognized by CTLs (e.g., as described in the Examples), one can make conservative amino acid substitutions to the amino acid sequence of the peptide, particularly at residues which are thought not to be direct contact points with the MHC molecule. For example, methods for identifying functional variants of HLA class II binding peptides are provided in a published PCT application of Strominger and Wucherpfennig (PCT/US96/03182). Peptides bearing one or more amino acid substitutions also can be tested for concordance with known HLA/MHC motifs prior to synthesis using, e.g. the computer program described by D'Amaro and Drijfhout (D'Amaro et al., *Human Immunol.* 43:13-18, 1995; Drijfhout et al., *Human Immunol.* 43:1-12, 1995). The substituted peptides can then be tested for binding to the MHC molecule and recognition by CTLs when bound to MHC. These variants can be tested for improved stability and are useful, *inter alia*, in vaccine compositions.

Conservative amino-acid substitutions in the amino acid sequence of cancer associated antigen polypeptides to produce functionally equivalent variants of cancer associated antigen polypeptides typically are made by alteration of a nucleic acid encoding a cancer associated antigen polypeptide. Such substitutions can be made by a variety of methods known to one of ordinary skill in the art. For example, amino acid substitutions may be made by PCR-directed mutation, site-directed mutagenesis according to the method of Kunkel (Kunkel, *Proc. Nat. Acad. Sci. U.S.A.* 82: 488-492, 1985), or by chemical synthesis of a gene encoding a cancer associated antigen polypeptide. Where amino acid substitutions are made to a small unique fragment of a cancer associated antigen polypeptide, such as an antigenic epitope recognized by autologous or allogeneic sera or cytolytic T lymphocytes, the substitutions can be made by directly synthesizing the peptide. The activity of functionally equivalent fragments of cancer associated antigen polypeptides can be tested by cloning the gene encoding the altered cancer associated antigen polypeptide into a bacterial or mammalian expression vector, introducing the vector into an appropriate host cell, expressing the altered cancer associated antigen polypeptide, and testing for a functional capability of the cancer associated antigen polypeptides as disclosed herein. Peptides which are chemically synthesized can be tested directly for function, e.g., for binding to antisera recognizing associated antigens.

The invention as described herein has a number of uses, some of which are described elsewhere herein. First, the invention permits isolation of the cancer associated antigen protein

molecules. A variety of methodologies well-known to the skilled practitioner can be utilized to obtain isolated cancer associated antigen molecules. The polypeptide may be purified from cells which naturally produce the polypeptide by chromatographic means or immunological recognition. Alternatively, an expression vector may be introduced into cells to cause production of the polypeptide. In another method, mRNA transcripts may be microinjected or otherwise introduced into cells to cause production of the encoded polypeptide. Translation of mRNA in cell-free extracts such as the reticulocyte lysate system also may be used to produce polypeptide. Those skilled in the art also can readily follow known methods for isolating cancer associated antigen polypeptides. These include, but are not limited to, immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography and immune-affinity chromatography.

The isolation and identification of cancer associated antigen genes also makes it possible for the artisan to diagnose a disorder characterized by expression of cancer associated antigens. These methods involve determining expression of one or more cancer associated antigen nucleic acids, and/or encoded cancer associated antigen polypeptides and/or peptides derived therefrom. In the former situation, such determinations can be carried out via any standard nucleic acid determination assay, including the polymerase chain reaction, or assaying with labeled hybridization probes. In the latter situation, such determinations can be carried out by screening patient antisera for recognition of the polypeptide.

The invention also makes it possible isolate proteins which bind to cancer associated antigens as disclosed herein, including antibodies and cellular binding partners of the cancer associated antigens. Additional uses are described further herein.

The invention also provides, in certain embodiments, "dominant negative" polypeptides derived from cancer associated antigen polypeptides. A dominant negative polypeptide is an inactive variant of a protein, which, by interacting with the cellular machinery, displaces an active protein from its interaction with the cellular machinery or competes with the active protein, thereby reducing the effect of the active protein. For example, a dominant negative receptor which binds a ligand but does not transmit a signal in response to binding of the ligand can reduce the biological effect of expression of the ligand. Likewise, a dominant negative catalytically-inactive kinase which interacts normally with target proteins but does not phosphorylate the target proteins can reduce phosphorylation of the target proteins in response to a cellular signal. Similarly, a dominant

negative transcription factor which binds to a promoter site in the control region of a gene but does not increase gene transcription can reduce the effect of a normal transcription factor by occupying promoter binding sites without increasing transcription.

The end result of the expression of a dominant negative polypeptide in a cell is a reduction in function of active proteins. One of ordinary skill in the art can assess the potential for a dominant negative variant of a protein, and using standard mutagenesis techniques to create one or more dominant negative variant polypeptides. For example, given the teachings contained herein of cancer associated antigens, especially those which are similar to known proteins which have known activities, one of ordinary skill in the art can modify the sequence of the cancer associated antigens by site-specific mutagenesis, scanning mutagenesis, partial gene deletion or truncation, and the like. See, e.g., U.S. Patent No. 5,580,723 and Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Second Edition, Cold Spring Harbor Laboratory Press, 1989. The skilled artisan then can test the population of mutagenized polypeptides for diminution in a selected and/or for retention of such an activity. Other similar methods for creating and testing dominant negative variants of a protein will be apparent to one of ordinary skill in the art.

The invention also involves agents such as polypeptides which bind to cancer associated antigen polypeptides. Such binding agents can be used, for example, in screening assays to detect the presence or absence of cancer associated antigen polypeptides and complexes of cancer associated antigen polypeptides and their binding partners and in purification protocols to isolated cancer associated antigen polypeptides and complexes of cancer associated antigen polypeptides and their binding partners. Such agents also can be used to inhibit the native activity of the cancer associated antigen polypeptides, for example, by binding to such polypeptides.

The invention, therefore, embraces peptide binding agents which, for example, can be antibodies or fragments of antibodies having the ability to selectively bind to cancer associated antigen polypeptides. Antibodies include polyclonal and monoclonal antibodies, prepared according to conventional methodology.

Significantly, as is well-known in the art, only a small portion of an antibody molecule, the paratope, is involved in the binding of the antibody to its epitope (see, in general, Clark, W.R. (1986) The Experimental Foundations of Modern Immunology Wiley & Sons, Inc., New York; Roitt, I. (1991) Essential Immunology, 7th Ed., Blackwell Scientific Publications, Oxford). The

pFc' and Fc regions, for example, are effectors of the complement cascade but are not involved in antigen binding. An antibody from which the pFc' region has been enzymatically cleaved, or which has been produced without the pFc' region, designated an F(ab')<sub>2</sub> fragment, retains both of the antigen binding sites of an intact antibody. Similarly, an antibody from which the Fc region has been enzymatically cleaved, or which has been produced without the Fc region, designated an Fab fragment, retains one of the antigen binding sites of an intact antibody molecule. Proceeding further, Fab fragments consist of a covalently bound antibody light chain and a portion of the antibody heavy chain denoted Fd. The Fd fragments are the major determinant of antibody specificity (a single Fd fragment may be associated with up to ten different light chains without altering antibody specificity) and Fd fragments retain epitope-binding ability in isolation.

Within the antigen-binding portion of an antibody, as is well-known in the art, there are complementarity determining regions (CDRs), which directly interact with the epitope of the antigen, and framework regions (FRs), which maintain the tertiary structure of the paratope (see, in general, Clark, 1986; Roitt, 1991). In both the heavy chain Fd fragment and the light chain of IgG immunoglobulins, there are four framework regions (FR1 through FR4) separated respectively by three complementarity determining regions (CDR1 through CDR3). The CDRs, and in particular the CDR3 regions, and more particularly the heavy chain CDR3, are largely responsible for antibody specificity.

It is now well-established in the art that the non-CDR regions of a mammalian antibody may be replaced with similar regions of conspecific or heterospecific antibodies while retaining the epitopic specificity of the original antibody. This is most clearly manifested in the development and use of "humanized" antibodies in which non-human CDRs are covalently joined to human FR and/or Fc/pFc' regions to produce a functional antibody. Thus, for example, PCT International Publication Number WO 92/04381 teaches the production and use of humanized murine RSV antibodies in which at least a portion of the murine FR regions have been replaced by FR regions of human origin. Such antibodies, including fragments of intact antibodies with antigen-binding ability, are often referred to as "chimeric" antibodies.

Thus, as will be apparent to one of ordinary skill in the art, the present invention also provides for F(ab')<sub>2</sub>, Fab, Fv and Fd fragments; chimeric antibodies in which the Fc and/or FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous

human or non-human sequences; chimeric F(ab')<sub>2</sub> fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; chimeric Fab fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; and chimeric Fd fragment antibodies in which the FR and/or CDR1 and/or CDR2 regions have been replaced by homologous human or non-human sequences. The present invention also includes so-called single chain antibodies.

Thus, the invention involves polypeptides of numerous size and type that bind specifically to cancer associated antigen polypeptides, and complexes of both cancer associated antigen polypeptides and their binding partners. These polypeptides may be derived also from sources other than antibody technology. For example, such polypeptide binding agents can be provided by degenerate peptide libraries which can be readily prepared in solution, in immobilized form or as phage display libraries. Combinatorial libraries also can be synthesized of peptides containing one or more amino acids. Libraries further can be synthesized of peptoids and non-peptide synthetic moieties.

Phage display can be particularly effective in identifying binding peptides useful according to the invention. Briefly, one prepares a phage library (using e.g. m13, fd, or lambda phage), displaying inserts from 4 to about 80 amino acid residues using conventional procedures. The inserts may represent, for example, a completely degenerate or biased array. One then can select phage-bearing inserts which bind to the cancer associated antigen polypeptide. This process can be repeated through several cycles of reselection of phage that bind to the cancer associated antigen polypeptide. Repeated rounds lead to enrichment of phage bearing particular sequences. DNA sequence analysis can be conducted to identify the sequences of the expressed polypeptides. The minimal linear portion of the sequence that binds to the cancer associated antigen polypeptide can be determined. One can repeat the procedure using a biased library containing inserts containing part or all of the minimal linear portion plus one or more additional degenerate residues upstream or downstream thereof. Yeast two-hybrid screening methods also may be used to identify polypeptides that bind to the cancer associated antigen polypeptides. Thus, the cancer associated antigen polypeptides of the invention, or a fragment thereof, can be used to screen peptide libraries, including phage display libraries, to identify and select peptide binding partners of the cancer

associated antigen polypeptides of the invention. Such molecules can be used, as described, for screening assays, for purification protocols, for interfering directly with the functioning of cancer associated antigen and for other purposes that will be apparent to those of ordinary skill in the art.

As detailed herein, the foregoing antibodies and other binding molecules may be used for example to identify tissues expressing protein or to purify protein. Antibodies also may be coupled to specific diagnostic labeling agents for imaging of cells and tissues that express cancer associated antigens or to therapeutically useful agents according to standard coupling procedures. Diagnostic agents include, but are not limited to, barium sulfate, iocetamic acid, iopanoic acid, ipodate calcium, diatrizoate sodium, diatrizoate meglumine, metrizamide, tyropanoate sodium and radiodiagnostics including positron emitters such as fluorine-18 and carbon-11, gamma emitters such as iodine-123, technitium-99m, iodine-131 and indium-111, nuclides for nuclear magnetic resonance such as fluorine and gadolinium. Other diagnostic agents useful in the invention will be apparent to one of ordinary skill in the art. As used herein, "therapeutically useful agents" include any therapeutic molecule which desirably is targeted selectively to a cell expressing one of the cancer antigens disclosed herein, including antineoplastic agents, radioiodinated compounds, toxins, other cytostatic or cytolytic drugs, and so forth. Antineoplastic therapeutics are well known and include: aminoglutethimide, azathioprine, bleomycin sulfate, busulfan, carmustine, chlorambucil, cisplatin, cyclophosphamide, cyclosporine, cytarabidine, dacarbazine, dactinomycin, daunorubicin, doxorubicin, taxol, etoposide, fluorouracil, interferon- $\alpha$ , lomustine, mercaptopurine, methotrexate, mitotane, procarbazine HCl, thioguanine, vinblastine sulfate and vincristine sulfate. Additional antineoplastic agents include those disclosed in Chapter 52, Antineoplastic Agents (Paul Calabresi and Bruce A. Chabner), and the introduction thereto, 1202-1263, of Goodman and Gilman's "The Pharmacological Basis of Therapeutics", Eighth Edition, 1990, McGraw-Hill, Inc. (Health Professions Division). Toxins can be proteins such as, for example, pokeweed anti-viral protein, cholera toxin, pertussis toxin, ricin, gelonin, abrin, diphtheria exotoxin, or *Pseudomonas* exotoxin. Toxin moieties can also be high energy-emitting radionuclides such as cobalt-60.

In the foregoing methods, antibodies prepared according to the invention also preferably are specific for the cancer associated antigen/MHC complexes described herein.

When "disorder" is used herein, it refers to any pathological condition where the cancer associated antigens are expressed. An example of such a disorder is cancer, breast, colon, gastric,



renal, prostate and lung cancers as particular examples.

Samples of tissue and/or cells for use in the various methods described herein can be obtained through standard methods such as tissue biopsy, including punch biopsy and cell scraping, and collection of blood or other bodily fluids by aspiration or other methods.

5 In certain embodiments of the invention, an immunoreactive cell sample is removed from a subject. By "immunoreactive cell" is meant a cell which can mature into an immune cell (such as a B cell, a helper T cell, or a cytolytic T cell) upon appropriate stimulation. Thus immunoreactive cells include CD34<sup>+</sup> hematopoietic stem cells, immature T cells and immature B cells. When it is desired to produce cytolytic T cells which recognize a cancer associated antigen, the  
10 immunoreactive cell is contacted with a cell which expresses a cancer associated antigen under conditions favoring production, differentiation and/or selection of cytolytic T cells; the differentiation of the T cell precursor into a cytolytic T cell upon exposure to antigen is similar to clonal selection of the immune system.

Some therapeutic approaches based upon the disclosure are premised on a response by a  
15 subject's immune system, leading to lysis of antigen presenting cells, such as breast cancer cells which present one or more cancer associated antigens. One such approach is the administration of autologous CTLs specific to a cancer associated antigen/MHC complex to a subject with abnormal cells of the phenotype at issue. It is within the ability of one of ordinary skill in the art to develop such CTLs *in vitro*. An example of a method for T cell differentiation is presented in International  
20 Application number PCT/US96/05607. Generally, a sample of cells taken from a subject, such as blood cells, are contacted with a cell presenting the complex and capable of provoking CTLs to proliferate. The target cell can be a transfectant, such as a COS cell of the type described herein. These transfectants present the desired complex of their surface and, when combined with a CTL of interest, stimulate its proliferation. COS cells, such as those used herein are widely available, as are  
25 other suitable host cells. Specific production of a CTL clone is described herein, and is well known in the art. The clonally expanded autologous CTLs then are administered to the subject.

Another method for selecting antigen-specific CTL clones has recently been described (Altman et al., *Science* 274:94-96, 1996; Dunbar et al., *Curr. Biol.* 8:413-416, 1998), in which fluorogenic tetramers of MHC class I molecule/peptide complexes are used to detect specific CTL  
30 clones. Briefly, soluble MHC class I molecules are folded *in vitro* in the presence of  $\beta_2$ -

microglobulin and a peptide antigen which binds the class I molecule. After purification, the MHC/peptide complex is purified and labeled with biotin. Tetramers are formed by mixing the biotinylated peptide-MHC complex with labeled avidin (e.g. phycoerythrin) at a molar ratio of 4:1. Tetramers are then contacted with a source of CTLs such as peripheral blood or lymph node. The tetramers bind CTLs which recognize the peptide antigen/MHC class I complex. Cells bound by the tetramers can be sorted by fluorescence activated cell sorting to isolate the reactive CTLs. The isolated CTLs then can be expanded *in vitro* for use as described herein.

To detail a therapeutic methodology, referred to as adoptive transfer (Greenberg, *J. Immunol.* 136(5): 1917, 1986; Riddel et al., *Science* 257: 238, 1992; Lynch et al, *Eur. J. Immunol.* 21: 1403-1410, 1991; Kast et al., *Cell* 59: 603-614, 1989), cells presenting the desired complex are combined with CTLs leading to proliferation of the CTLs specific thereto. The proliferated CTLs are then administered to a subject with a cellular abnormality which is characterized by certain of the abnormal cells presenting the particular complex. The CTLs then lyse the abnormal cells, thereby achieving the desired therapeutic goal.

The foregoing therapy assumes that at least some of the subject's abnormal cells present the relevant HLA cancer associated antigen complex. This can be determined very easily, as the art is very familiar with methods for identifying cells which present a particular HLA molecule, as well as how to identify cells expressing DNA of the pertinent sequences, in this case a cancer associated antigen sequence. Once cells presenting the relevant complex are identified via the foregoing screening methodology, they can be combined with a sample from a patient, where the sample contains CTLs. If the complex presenting cells are lysed by the mixed CTL sample, then it can be assumed that a cancer associated antigen is being presented, and the subject is an appropriate candidate for the therapeutic approaches set forth *supra*.

Adoptive transfer is not the only form of therapy that is available in accordance with the invention. CTLs can also be provoked *in vivo*, using a number of approaches. One approach is the use of non-proliferative cells expressing the complex. The cells used in this approach may be those that normally express the complex, such as irradiated tumor cells or cells transfected with one or both of the genes necessary for presentation of the complex (i.e. the antigenic peptide and the presenting HLA molecule). Chen et al. (*Proc. Natl. Acad. Sci. USA* 88: 110-114, 1991) exemplifies this approach, showing the use of transfected cells expressing HPV E7 peptides in a therapeutic

regime. Various cell types may be used. Similarly, vectors carrying one or both of the genes of interest may be used. Viral or bacterial vectors are especially preferred. For example, nucleic acids which encode a breast cancer associated antigen polypeptide or peptide may be operably linked to promoter and enhancer sequences which direct expression of the cancer associated antigen polypeptide or peptide in certain tissues or cell types. The nucleic acid may be incorporated into an expression vector. Expression vectors may be unmodified extrachromosomal nucleic acids, plasmids or viral genomes constructed or modified to enable insertion of exogenous nucleic acids, such as those encoding cancer associated antigen, as described elsewhere herein. Nucleic acids encoding a cancer associated antigen also may be inserted into a retroviral genome, thereby facilitating integration of the nucleic acid into the genome of the target tissue or cell type. In these systems, the gene of interest is carried by a microorganism, e.g., a Vaccinia virus, retrovirus or adenovirus, and the materials de facto "infect" host cells. The cells which result present the complex of interest, and are recognized by autologous CTLs, which then proliferate.

A similar effect can be achieved by combining the cancer associated antigen or a stimulatory fragment thereof with an adjuvant to facilitate incorporation into antigen presenting cells *in vivo*. The breast cancer associated antigen polypeptide is processed to yield the peptide partner of the HLA molecule while a cancer associated antigen peptide may be presented without the need for further processing. Generally, subjects can receive an intradermal injection of an effective amount of the cancer associated antigen. Initial doses can be followed by booster doses, following immunization protocols standard in the art. Preferred cancer associated antigens include those found to react with allogeneic cancer antisera, such as the nucleic acids (and encoded polypeptides and peptides) of SEQ ID NO:31,33 and 34 and others, for example, shown in the examples below.

The invention involves the use of various materials disclosed herein to "immunize" subjects or as "vaccines". As used herein, "immunization" or "vaccination" means increasing or activating an immune response against an antigen. It does not require elimination or eradication of a condition but rather contemplates the clinically favorable enhancement of an immune response toward an antigen. Generally accepted animal models can be used for testing of immunization against breast cancer using a cancer associated antigen nucleic acid. For example, cancer cells can be introduced into a mouse to create a tumor, and one or more cancer associated antigen nucleic acids can be delivered by the methods described herein. The effect on the cancer cells (e.g., reduction of tumor

size) can be assessed as a measure of the effectiveness of the cancer associated antigen nucleic acid immunization. Of course, testing of the foregoing animal model using more conventional methods for immunization include the administration of one or more cancer associated antigen polypeptides or peptides derived therefrom, optionally combined with one or more adjuvants and/or cytokines to boost the immune response. Methods for immunization, including formulation of a vaccine composition and selection of doses, route of administration and the schedule of administration (e.g. primary and one or more booster doses), are well known in the art. The tests also can be performed in humans, where the end point is to test for the presence of enhanced levels of circulating CTLs against cells bearing the antigen, to test for levels of circulating antibodies against the antigen, to test for the presence of cells expressing the antigen and so forth.

As part of the immunization compositions, one or more cancer associated antigens or stimulatory fragments thereof are administered with one or more adjuvants to induce an immune response or to increase an immune response. An adjuvant is a substance incorporated into or administered with antigen which potentiates the immune response. Adjuvants may enhance the immunological response by providing a reservoir of antigen (extracellularly or within macrophages), activating macrophages and stimulating specific sets of lymphocytes. Adjuvants of many kinds are well known in the art. Specific examples of adjuvants include monophosphoryl lipid A (MPL, SmithKline Beecham), a congener obtained after purification and acid hydrolysis of *Salmonella minnesota* Re 595 lipopolysaccharide; saponins including QS21 (SmithKline Beecham), a pure QA-21 saponin purified from *Quillja saponaria* extract; DQS21, described in PCT application WO96/33739 (SmithKline Beecham); QS-7, QS-17, QS-18, and QS-L1 (So et al., *Mol. Cells* 7:178-186, 1997); incomplete Freund's adjuvant; complete Freund's adjuvant; montanide; and various water-in-oil emulsions prepared from biodegradable oils such as squalene and/or tocopherol. Preferably, the peptides are administered mixed with a combination of DQS21/MPL. The ratio of DQS21 to MPL typically will be about 1:10 to 10:1, preferably about 1:5 to 5:1 and more preferably about 1:1. Typically for human administration, DQS21 and MPL will be present in a vaccine formulation in the range of about 1 µg to about 100 µg. Other adjuvants are known in the art and can be used in the invention (see, e.g. Goding, *Monoclonal Antibodies: Principles and Practice*, 2nd Ed., 1986). Methods for the preparation of mixtures or emulsions of peptide and adjuvant are well known to those of skill in the art of vaccination.

Other agents which stimulate the immune response of the subject can also be administered to the subject. For example, other cytokines are also useful in vaccination protocols as a result of their lymphocyte regulatory properties. Many other cytokines useful for such purposes will be known to one of ordinary skill in the art, including interleukin-12 (IL-12) which has been shown to enhance the protective effects of vaccines (*see, e.g., Science* 268: 1432-1434, 1995), GM-CSF and IL-18. Thus cytokines can be administered in conjunction with antigens and adjuvants to increase the immune response to the antigens.

There are a number of immune response potentiating compounds that can be used in vaccination protocols. These include costimulatory molecules provided in either protein or nucleic acid form. Such costimulatory molecules include the B7-1 and B7-2 (CD80 and CD86 respectively) molecules which are expressed on dendritic cells (DC) and interact with the CD28 molecule expressed on the T cell. This interaction provides costimulation (signal 2) to an antigen/MHC/TCR stimulated (signal 1) T cell, increasing T cell proliferation and effector function. B7 also interacts with CTLA4 (CD152) on T cells and studies involving CTLA4 and B7 ligands indicate that the B7-CTLA4 interaction can enhance antitumor immunity and CTL proliferation, Zheng P., et al. *PNAS* 95 (11) 6284-6289 (1998).

B7 typically is not expressed on tumor cells so they are not efficient antigen presenting cells (APCs) for T cells. Induction of B7 expression would enable the tumor cells to stimulate more efficiently CTL proliferation and effector function. A combination of B7/IL-6/IL-12 costimulation has been shown to induce IFN-gamma and a Th1 cytokine profile in the T cell population leading to further enhanced T cell activity, Gajewski et al., *J. Immunol.*, 154:5637-5648 (1995). Tumor cell transfection with B7 has been discussed in relation to *in vitro* CTL expansion for adoptive transfer immunotherapy by Wang et al., *J Immunol.*, 19:1-8 (1986). Other delivery mechanisms for the B7 molecule would include nucleic acid (naked DNA) immunization Kim J., et al. *Nat Biotechnol.*, 15:7:641-646 (1997) and recombinant viruses such as adeno and pox (Wendtner et al., *Gene Ther.*, 4:7:726-735 (1997)). These systems are all amenable to the construction and use of expression cassettes for the coexpression of B7 with other molecules of choice such as the antigens or fragment(s) of antigens discussed herein (including polytopes) or cytokines. These delivery systems can be used for induction of the appropriate molecules *in vitro* and for *in vivo* vaccination situations. The use of anti-CD28 antibodies to directly stimulate T cells *in vitro* and *in vivo* could also be

considered.

Lymphocyte function associated antigen-3 (LFA-3) is expressed on APCs and some tumor cells and interacts with CD2 expressed on T cells. This interaction induces T cell IL-2 and IFN-gamma production and can thus complement but not substitute, the B7/CD28 costimulatory interaction, Parra et al., *J. Immunol.*, 158:637-642 (1997), Fenton et al., *J. Immunother*, 21:2:95-108 (1989).

Lymphocyte function associated antigen-1 (LFA-1) is expressed on leukocytes and interacts with ICAM-1 expressed on APCs and some tumor cells. This interaction induces T cell IL-2 and IFN-gamma production and can thus complement but not substitute, the B7/CD28 costimulatory interaction, Fenton et al., *J. Immunother*, 21:2:95-108 (1998). LFA-1 is thus a further example of a costimulatory molecule that could be provided in a vaccination protocol in the various ways discussed above for B7.

Complete CTL activation and effector function requires Th cell help through the interaction between the Th cell CD40L (CD40 ligand) molecule and the CD40 molecule expressed by DCS, Ridge et al., *Nature*, 393:474 (1998), Bennett et al., *Nature*, 393:478 (1998), Schoenberger et al., *Nature*, 393:480 (1998). This mechanism of this costimulatory signal is likely to involve upregulation of B7 and associated IL-6/IL-12 production by the DC (APC). The CD40-CD40L interaction thus complements the signal 1 (antigen/MHC-TCR) and signal 2 (B7-CD28) interactions.

The use of anti-CD40 antibodies to stimulate DC cells directly, would be expected to enhance a response to tumor antigens which are normally encountered outside of an inflammatory context or are presented by non-professional APCs (tumor cells). In these situations Th help and B7 costimulation signals are not provided. This mechanism might be used in the context of antigen pulsed DC based therapies or in situations where Th epitopes have not been defined within known TRA precursors.

A cancer associated antigen polypeptide, or a fragment thereof, also can be used to isolate their native binding partners. Isolation of such binding partners may be performed according to well-known methods. For example, isolated cancer associated antigen polypeptides can be attached to a substrate (e.g., chromatographic media, such as polystyrene beads, or a filter), and then a solution suspected of containing the binding partner may be applied to the substrate. If a binding partner which can interact with cancer associated antigen polypeptides is present in the solution,

then it will bind to the substrate-bound cancer associated antigen polypeptide. The binding partner then may be isolated.

It will also be recognized that the invention embraces the use of the cancer associated antigen cDNA sequences in expression vectors, as well as to transfect host cells and cell lines, be these  
5 prokaryotic (e.g., *E. coli*), or eukaryotic (e.g., dendritic cells, B cells, CHO cells, COS cells, yeast expression systems and recombinant baculovirus expression in insect cells). Especially useful are mammalian cells such as human, mouse, hamster, pig, goat, primate, etc. They may be of a wide variety of tissue types, and include primary cells and cell lines. Specific examples include keratinocytes, peripheral blood leukocytes, bone marrow stem cells and embryonic stem cells. The  
10 expression vectors require that the pertinent sequence, i.e., those nucleic acids described *supra*, be operably linked to a promoter.

The invention also contemplates delivery of nucleic acids, polypeptides or peptides for vaccination. Delivery of polypeptides and peptides can be accomplished according to standard vaccination protocols which are well known in the art. In another embodiment, the delivery of  
15 nucleic acid is accomplished by *ex vivo* methods, i.e. by removing a cell from a subject, genetically engineering the cell to include a breast cancer associated antigen, and reintroducing the engineered cell into the subject. One example of such a procedure is outlined in U.S. Patent 5,399,346 and in exhibits submitted in the file history of that patent, all of which are publicly available documents. In general, it involves introduction *in vitro* of a functional copy of a gene into a cell(s) of a subject, and  
20 returning the genetically engineered cell(s) to the subject. The functional copy of the gene is under operable control of regulatory elements which permit expression of the gene in the genetically engineered cell(s). Numerous transfection and transduction techniques as well as appropriate expression vectors are well known to those of ordinary skill in the art, some of which are described in PCT application WO95/00654. *In vivo* nucleic acid delivery using vectors such as viruses and  
25 targeted liposomes also is contemplated according to the invention.

In preferred embodiments, a virus vector for delivering a nucleic acid encoding a cancer associated antigen is selected from the group consisting of adenoviruses, adeno-associated viruses, poxviruses including vaccinia viruses and attenuated poxviruses, Semliki Forest virus, Venezuelan equine encephalitis virus, retroviruses, Sindbis virus, and Ty virus-like particle. Examples of  
30 viruses and virus-like particles which have been used to deliver exogenous nucleic acids include:

replication-defective adenoviruses (e.g., Xiang et al., *Virology* 219:220-227, 1996; Eloit et al., *J. Virol* 7:5375-5381, 1997; Chengalvala et al., *Vaccine* 15:335-339, 1997), a modified retrovirus (Townsend et al., *J. Virol.* 71:3365-3374, 1997), a nonreplicating retrovirus (Irwin et al., *J. Virol.* 68:5036-5044, 1994), a replication defective Semliki Forest virus (Zhao et al., *Proc. Natl. Acad. Sci. USA* 92:3009-3013, 1995), canarypox virus and highly attenuated vaccinia virus derivative (Paoletti, *Proc. Natl. Acad. Sci. USA* 93:11349-11353, 1996), non-replicative vaccinia virus (Moss, *Proc. Natl. Acad. Sci. USA* 93:11341-11348, 1996), replicative vaccinia virus (Moss, *Dev. Biol. Stand.* 82:55-63, 1994), Venezuelan equine encephalitis virus (Davis et al., *J. Virol.* 70:3781-3787, 1996), Sindbis virus (Pugachev et al., *Virology* 212:587-594, 1995), and Ty virus-like particle (Allsopp et al., *Eur J. Immunol* 26:1951-1959, 1996). In preferred embodiments, the virus vector is an adenovirus.

Another preferred virus for certain applications is the adeno-associated virus, a double-stranded DNA virus. The adeno-associated virus is capable of infecting a wide range of cell types and species and can be engineered to be replication-deficient. It further has advantages, such as heat and lipid solvent stability, high transduction frequencies in cells of diverse lineages, including hematopoietic cells, and lack of superinfection inhibition thus allowing multiple series of transductions. The adeno-associated virus can integrate into human cellular DNA in a site-specific manner, thereby minimizing the possibility of insertional mutagenesis and variability of inserted gene expression. In addition, wild-type adeno-associated virus infections have been followed in tissue culture for greater than 100 passages in the absence of selective pressure, implying that the adeno-associated virus genomic integration is a relatively stable event. The adeno-associated virus can also function in an extrachromosomal fashion.

In general, other preferred viral vectors are based on non-cytopathic eukaryotic viruses in which non-essential genes have been replaced with the gene of interest. Non-cytopathic viruses include retroviruses, the life cycle of which involves reverse transcription of genomic viral RNA into DNA with subsequent proviral integration into host cellular DNA. Adenoviruses and retroviruses have been approved for human gene therapy trials. In general, the retroviruses are replication-deficient (i.e., capable of directing synthesis of the desired proteins, but incapable of manufacturing an infectious particle). Such genetically altered retroviral expression vectors have general utility for the high-efficiency transduction of genes *in vivo*. Standard protocols for



producing replication-deficient retroviruses (including the steps of incorporation of exogenous genetic material into a plasmid, transfection of a packaging cell lined with plasmid, production of recombinant retroviruses by the packaging cell line, collection of viral particles from tissue culture media, and infection of the target cells with viral particles) are provided in Kriegler, M., "Gene Transfer and Expression, A Laboratory Manual," W.H. Freeman C.O., New York (1990) and Murry, E.J. Ed. "Methods in Molecular Biology," vol. 7, Humana Press, Inc., Clifton, New Jersey (1991).

Preferably the foregoing nucleic acid delivery vectors: (1) contain exogenous genetic material that can be transcribed and translated in a mammalian cell and that can induce an immune response in a host, and (2) contain on a surface a ligand that selectively binds to a receptor on the surface of a target cell, such as a mammalian cell, and thereby gains entry to the target cell.

Various techniques may be employed for introducing nucleic acids of the invention into cells, depending on whether the nucleic acids are introduced *in vitro* or *in vivo* in a host. Such techniques include transfection of nucleic acid- $\text{CaPO}_4$  precipitates, transfection of nucleic acids associated with DEAE, transfection or infection with the foregoing viruses including the nucleic acid of interest, liposome mediated transfection, and the like. For certain uses, it is preferred to target the nucleic acid to particular cells. In such instances, a vehicle used for delivering a nucleic acid of the invention into a cell (e.g., a retrovirus, or other virus; a liposome) can have a targeting molecule attached thereto. For example, a molecule such as an antibody specific for a surface membrane protein on the target cell or a ligand for a receptor on the target cell can be bound to or incorporated within the nucleic acid delivery vehicle. Preferred antibodies include antibodies which selectively bind a cancer associated antigen, alone or as a complex with a MHC molecule.

Especially preferred are monoclonal antibodies. Where liposomes are employed to deliver the nucleic acids of the invention, proteins which bind to a surface membrane protein associated with endocytosis may be incorporated into the liposome formulation for targeting and/or to facilitate uptake. Such proteins include capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half life, and the like. Polymeric delivery systems also have been used successfully to deliver nucleic acids into cells, as is known by those skilled in the art. Such systems even permit oral delivery of nucleic acids.

When administered, the therapeutic compositions of the present invention can be

administered in pharmaceutically acceptable preparations. Such preparations may routinely contain pharmaceutically acceptable concentrations of salt, buffering agents, preservatives, compatible carriers, supplementary immune potentiating agents such as adjuvants and cytokines and optionally other therapeutic agents.

5           The therapeutics of the invention can be administered by any conventional route, including injection or by gradual infusion over time. The administration may, for example, be oral, intravenous, intraperitoneal, intramuscular, intracavity, subcutaneous, or transdermal. When antibodies are used therapeutically, a preferred route of administration is by pulmonary aerosol. Techniques for preparing aerosol delivery systems containing antibodies are well known to those of  
10 skill in the art. Generally, such systems should utilize components which will not significantly impair the biological properties of the antibodies, such as the paratope binding capacity (see, for example, Sciarra and Cutie, "Aerosols," in Remington's Pharmaceutical Sciences, 18th edition, 1990, pp 1694-1712; incorporated by reference). Those of skill in the art can readily determine the various parameters and conditions for producing antibody aerosols without resort to undue  
15 experimentation. When using antisense preparations of the invention, slow intravenous administration is preferred.

          The compositions of the invention are administered in effective amounts. An "effective amount" is that amount of a cancer associated antigen composition that alone, or together with further doses, produces the desired response, e.g. increases an immune response to the cancer  
20 associated antigen. In the case of treating a particular disease or condition characterized by expression of one or more cancer associated antigens, such as cancer, the desired response is inhibiting the progression of the disease. This may involve only slowing the progression of the disease temporarily, although more preferably, it involves halting the progression of the disease permanently. This can be monitored by routine methods or can be monitored according to  
25 diagnostic methods of the invention discussed herein. The desired response to treatment of the disease or condition also can be delaying the onset or even preventing the onset of the disease or condition.

          Such amounts will depend, of course, on the particular condition being treated, the severity of the condition, the individual patient parameters including age, physical condition, size and  
30 weight, the duration of the treatment, the nature of concurrent therapy (if any), the specific route of

administration and like factors within the knowledge and expertise of the health practitioner. These factors are well known to those of ordinary skill in the art and can be addressed with no more than routine experimentation. It is generally preferred that a maximum dose of the individual components or combinations thereof be used, that is, the highest safe dose according to sound medical judgment. It will be understood by those of ordinary skill in the art, however, that a patient may insist upon a lower dose or tolerable dose for medical reasons, psychological reasons or for virtually any other reasons.

The pharmaceutical compositions used in the foregoing methods preferably are sterile and contain an effective amount of breast cancer associated antigen or nucleic acid encoding cancer associated antigen for producing the desired response in a unit of weight or volume suitable for administration to a patient. The response can, for example, be measured by determining the immune response following administration of the cancer associated antigen composition via a reporter system as described herein, by measuring downstream effects such as gene expression, or by measuring the physiological effects of the breast cancer associated antigen composition, such as regression of a tumor or decrease of disease symptoms. Other assays will be known to one of ordinary skill in the art and can be employed for measuring the level of the response.

The doses of cancer associated antigen compositions (e.g., polypeptide, peptide, antibody, cell or nucleic acid) administered to a subject can be chosen in accordance with different parameters, in particular in accordance with the mode of administration used and the state of the subject. Other factors include the desired period of treatment. In the event that a response in a subject is insufficient at the initial doses applied, higher doses (or effectively higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits.

In general, for treatments for eliciting or increasing an immune response, doses of cancer associated antigen are formulated and administered in doses between 1 ng and 1 mg, and preferably between 10 ng and 100  $\mu$ g, according to any standard procedure in the art. Where nucleic acids encoding cancer associated antigen of variants thereof are employed, doses of between 1 ng and 0.1 mg generally will be formulated and administered according to standard procedures. Other protocols for the administration of cancer associated antigen compositions will be known to one of ordinary skill in the art, in which the dose amount, schedule of injections, sites of injections, mode of administration (e.g., intra-tumoral) and the like vary from the foregoing. Administration of cancer

associated antigen compositions to mammals other than humans, e.g. for testing purposes or veterinary therapeutic purposes, is carried out under substantially the same conditions as described above.

As part of the immunization compositions, the peptide antigens are administered with one or more adjuvants to induce an immune response or to increase an immune response. An adjuvant is a substance incorporated into or administered with antigen which potentiates the immune response. Adjuvants may enhance the immunological response by providing a reservoir of antigen (extracellularly or within macrophages), activating macrophages and stimulating specific sets of lymphocytes. Adjuvants of many kinds are well known in the art. Specific examples of adjuvants include monophosphoryl lipid A (MPL, SmithKline Beecham), a congener obtained after purification and acid hydrolysis of *Salmonella minnesota* Re 595 lipopolysaccharide; saponins including QS21 (SmithKline Beecham), a pure QA-21 saponin purified from *Quillja saponaria* extract; DQS21, described in PCT application WO96/33739 (SmithKline Beecham); QS-7, QS-17, QS-18, and QS-L1 (So et al., *Mol. Cells* 7:178-186, 1997); incomplete Freund's adjuvant; complete Freund's adjuvant; montanide; and various water-in-oil emulsions prepared from biodegradable oils such as squalene and/or tocopherol. Other adjuvants are known in the art and can be used in the invention (see, e.g. Goding, *Monoclonal Antibodies: Principles and Practice*, 2nd Ed., 1986). Methods for the preparation of mixtures or emulsions of peptide and adjuvant are well known to those of skill in the art of vaccination.

Where cancer associated antigen peptides are used for vaccination, modes of administration which effectively deliver the cancer associated antigen and adjuvant, such that an immune response to the antigen is increased, can be used. For administration of a cancer associated antigen peptide in adjuvant, preferred methods include intradermal, intravenous, intramuscular and subcutaneous administration. Although these are preferred embodiments, the invention is not limited by the particular modes of administration disclosed herein. Standard references in the art (e.g., *Remington's Pharmaceutical Sciences*, 18th edition, 1990) provide modes of administration and formulations for delivery of immunogens with adjuvant or in a non-adjuvant carrier.

When administered, the pharmaceutical preparations of the invention are applied in pharmaceutically-acceptable amounts and in pharmaceutically-acceptable compositions. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the

effectiveness of the biological activity of the active ingredients. Such preparations may routinely contain salts, buffering agents, preservatives, compatible carriers, and optionally other therapeutic agents. When used in medicine, the salts should be pharmaceutically acceptable, but non-pharmaceutically acceptable salts may conveniently be used to prepare pharmaceutically-acceptable salts thereof and are not excluded from the scope of the invention. Such pharmacologically and pharmaceutically-acceptable salts include, but are not limited to, those prepared from the following acids: hydrochloric, hydrobromic, sulfuric, nitric, phosphoric, maleic, acetic, salicylic, citric, formic, malonic, succinic, and the like. Also, pharmaceutically-acceptable salts can be prepared as alkaline metal or alkaline earth salts, such as sodium, potassium or calcium salts.

A breast cancer associated antigen composition may be combined, if desired, with a pharmaceutically-acceptable carrier. The term "pharmaceutically-acceptable carrier" as used herein means one or more compatible solid or liquid fillers, diluents or encapsulating substances which are suitable for administration into a human. The term "carrier" denotes an organic or inorganic ingredient, natural or synthetic, with which the active ingredient is combined to facilitate the application. The components of the pharmaceutical compositions also are capable of being co-mingled with the molecules of the present invention, and with each other, in a manner such that there is no interaction which would substantially impair the desired pharmaceutical efficacy.

The pharmaceutical compositions may contain suitable buffering agents, including: acetic acid in a salt; citric acid in a salt; boric acid in a salt; and phosphoric acid in a salt.

The pharmaceutical compositions also may contain, optionally, suitable preservatives, such as: benzalkonium chloride; chlorobutanol; parabens and thimerosal.

The pharmaceutical compositions may conveniently be presented in unit dosage form and may be prepared by any of the methods well-known in the art of pharmacy. All methods include the step of bringing the active agent into association with a carrier which constitutes one or more accessory ingredients. In general, the compositions are prepared by uniformly and intimately bringing the active compound into association with a liquid carrier, a finely divided solid carrier, or both, and then, if necessary, shaping the product.

Compositions suitable for oral administration may be presented as discrete units, such as

capsules, tablets, lozenges, each containing a predetermined amount of the active compound. Other compositions include suspensions in aqueous liquids or non-aqueous liquids such as a syrup, elixir or an emulsion.

Compositions suitable for parenteral administration conveniently comprise a sterile aqueous or non-aqueous preparation of breast cancer associated antigen polypeptides or nucleic acids, which is preferably isotonic with the blood of the recipient. This preparation may be formulated according to known methods using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation also may be a sterile injectable solution or suspension in a non-toxic parenterally-acceptable diluent or solvent, for example, as a solution in 1,3-butane diol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono-or di-glycerides. In addition, fatty acids such as oleic acid may be used in the preparation of injectables. Carrier formulation suitable for oral, subcutaneous, intravenous, intramuscular, etc. administrations can be found in *Remington's Pharmaceutical Sciences*, Mack Publishing Co., Easton, PA.

### Examples

#### **Example 1: Preparation of breast cancer cDNA expression libraries**

Step 1: Purification of total RNA from tumors.

Total RNA was isolated from tumor samples using the guanidium thiocyanate-phenol-chloroform extraction protocol described by Chomczynski and Sacci (*Anal. Biochem.* 162:156-159, 1987).

Step 2: Purification of mRNA.

A Dynabeads mRNA isolation kit (Dynal, Cat.No. 610.01) was used to isolate mRNA from the pool of total RNA isolated in step 1 above according to the manufacturer's instructions.

Step 3: cDNA synthesis.

cDNA synthesis was performed using a ZAP-cDNA synthesis Kit (Stratagene, La Jolla CA; Cat. No. 200400) according to the manufacturer's protocol. A specific linker-primer which contains a XbaI cloning site was designed and used in this protocol, to facilitate subcloning into TriplEx

vector. The sequence of the primer was:

GAGAGAGAGAGAGAGAGAGAAGTCGACTCTAGATTTTTTTTTTTTTTTTTTTT-Xba 1 site

Step 4: Ligation into the TriplEx vector arms.

5 The cDNAs generated in step 3 above were ligated into TriplEx vector arms (Clontech, Palo Alto, CA; Cat. No. 6162-1); the arms were predigested with EcoR I/Xba I.

Step 5: Packaging into phages with Gigapack III kit.

The ligation mix (TriplEx/cDNA) from step 4 was packed into phages using the Gigapack III Gold Cloning Kit (Stratagene, Cat. N.200450) according to the protocol supplied with the kit.

10 Step 6: Titering and amplification of generated libraries was performed according to the Stratagene protocols.

The foregoing protocol was used to prepare several libraries from tumor sample of different patients. Some libraries were prepared using the UNI-ZAP XR vector system (Stratagene) according to the manufacturer's protocol, and some using the TriplEx system as described above.

Table 2

UNI-ZAP Libraries		
Code for tumors	Titer of the library	Histopathological diagnosis
HBR173	$1.8 \times 10^6$ pfu	Ductal Carcinoma, Grade III
HBR184	$3.5 \times 10^6$ pfu	Invasive Ductal Carcinoma, Grade II
TriplEx libraries		
Code for tumors	Titer of the library	Histopathological diagnosis
HBR173	$2.3 \times 10^6$ pfu	Ductal Carcinoma, Grade III
HBR184	$1.1 \times 10^6$ pfu	Invasive Ductal Carcinoma, Grade II
HBR257	$2.5 \times 10^6$ pfu	Invasive Ductal Carcinoma, Grade II
HBR297	$4.0 \times 10^6$ pfu	Ductal Carcinoma, Grade II
HBR248	$1.0 \times 10^6$ pfu	Invasive Ductal Carcinoma with Vascular Permeation, Grade III

HBR271	2.5 x 10 <sup>6</sup> pfu	Medullary Carcimoma
HBR263	10.0 x 10 <sup>6</sup> pfu	Inv. Pleiomorphic Lobular Carcinoma, Grade II

5 All libraries were screened with the exception of HBR173 (no autologous serum). No serum-positive clones were found by screening HBR271 library.

### Example 2: Immunoscreening

10 Sera was obtained from donors undergoing routine diagnostic and therapeutic procedures. It was stored at - 70°C prior to absorption. Sera, at a dilution of 1:10 in Tris buffered saline (TBS, pH 7.5), was sequentially passed through Sepharose 4B columns which had been coupled to lysates from *E. coli* Y1090 and bacteriophage infected *E. coli* BNN97 (5 Prime 3 Prime, Inc. Boulder, Co.). Final serum dilutions were prepared in 0.2% non-fat dried milk/TBS (NFDM) and stored at 4°C. Library screening was performed as described by Sahin et al. (*Proc. Natl. Acad. Sci. USA* 92:11810-11813, 1995) with following modifications. Recombinant phage at a concentration of 4 x 10<sup>3</sup> per 15 cm plate were amplified for 6 hours and transferred to nitrocellulose membranes for an additional 15 hours at 37°C. Membranes were then blocked with 5% NFDM. As an alternative to generation of IgG subtracted libraries, membranes were pre-screened in a 1:2000 dilution of peroxidase conjugated, Fc fragment specific, goat anti-human IgG (Jackson ImmunoResearch Laboratories Inc., West Grove, PA) for 1 hour at room temperature. Color was developed with 3,3'-diaminobenzidine tetrahydrochloride and IgG encoding clones were scored. Membranes were then incubated in a 1:100 dilution of absorbed autologous sera for 15 hours at room temperature. Following serum exposure, filters were incubated in a 1:3000 dilution of alkaline phosphatase conjugated, Fc fragment specific, goat anti-human IgG (Jackson ImmunoResearch Laboratories Inc.) for 1 hour at room temperature and processed for 4-nitro blue tetrazolium chloride/5-bromo-4-chloro- 3-indolyl-phosphate color development. Serum positive clones were subcloned and retested for serum reactivity as above except nitrocellulose transfer was decreased to 3 hours. For the determination of allogeneic serum reactivity, plates containing an equal number of serum positive clones and negative control plaques were similarly processed less the IgG prescreening steps. A minimum of 5 x 10<sup>5</sup> recombinants were screened per cDNA library, a number



which approximates a point at which the likelihood of repeat isolations of previously identified clones outweigh the prospect of identifying new clones.

### Example 3: DNA Sequencing

- 5 Phage cDNA clones were converted to pBKCMV phagemid forms by in vivo excision. Plasmid DNA was purified on Qiaprep spin columns (Qiagen Inc. Chatsworth, CA) and subjected to EcoRI/XbaI restriction enzyme digestion. Clones representing different cDNA inserts were sequenced at Cornell University DNA services (Ithaca, NY) using an ABI Prism (Perkin Elmer) automated DNA sequencer. The sequences of the clones were compared with sequences in
- 10 GenBank and HGI databases to detect homologous nucleic acid and/or protein sequences. The following table lists exemplary related sequences.

Table 3: Sequences Related to Breast Cancer Associated Antigen Clones

Clone	Nucleotide Homology	Clone	Nucleotide Homology	Clone	Nucleotide Homology
LONY-Br-1	L34543	LONY-Br-23	AA262134, U74628	LONY-Br-44	D15057
LONY-Br-2	S75417	LONY-Br-24	AA282633	LONY-Br-45	AB000815
LONY-Br-3	J05211	LONY-Br-25	M62324	LONY-Br-46	L04733
LONY-Br-4	X15187	LONY-Br-26	M99389	LONY-Br-47	X88791
LONY-Br-5	X62083	LONY-Br-27	X79389	LONY-Br-48	AF000430
LONY-Br-6	J04965	LONY-Br-28	D44466	LONY-Br-49	none
LONY-Br-7	D63784	LONY-Br-29	M33197	LONY-Br-50	AA226732
LONY-Br-8	U11292	LONY-Br-30	M17886	LONY-Br-51	AA046574
LONY-Br-9	HSB06D102	LONY-Br-31	L38941	LONY-Br-52	none
LONY-Br-10	none	LONY-Br-32	X17644	LONY-Br-53	AB002307
LONY-Br-11	none	LONY-Br-33	X75342	92	AA127328
LONY-Br-12	AA430998	LONY-Br-33	X75342	101	AA167314
LONY-Br-13	D83032	LONY-Br-34	U43368	102	AA508139
LONY-Br-14	AA034417	LONY-Br-35	X15882	107	none
LONY-Br-15	AA167070	LONY-Br-37	AA121558	109	AA220229

LONY-Br-16	none	LONY-Br-38	AA211771	110	W67775
LONY-Br-17	AA161103	LONY-Br-39	AA367417	111	AA280070
LONY-Br-19	R13835	LONY-Br-40	AA188052	112	AF004292
LONY-Br-20	HUMORF003	LONY-Br-41	THC83518	131	none
LONY-Br-21	S74572	LONY-Br-42	none	143	AA481578
LONY-Br-22	AA070233	LONY-Br-43	HU35246	162	AA481578

#### Example 4: Reverse transcriptase (RT) PCR and Rapid Amplification of cDNA Ends (RACE)

The mRNA expression pattern of selected cDNA clones was determined by RT-PCR using a panel of normal tissue RNA. This test panel consisted of lung, testis, small intestine, colon, breast, liver, and placenta, and was purchased from Clontech Laboratories Inc. (Palo Alto, CA). Colon tumor RNA was also included in this panel and was prepared as described above. As a control for genomic DNA contamination, all cDNA synthesis reactions were set up in duplicate with the additional sample lacking reverse transcriptase. Gene specific PCR primers were designed to amplify 5' fragments of 300-400 bp and were purchased commercially (Gibco BRL, Grand Island, NY). PCR reactions were undertaken at an annealing temperature of 68°C using a Perkin Elmer thermal cycler. In certain cases, RT-PCR products were subcloned into the pCR2.1 plasmid vector (Invitrogen) and multiple clones were subjected to DNA sequencing as described. 5' and 3' RACE reactions were undertaken using gene specific and adapter primers in conjunction with Marathon Ready normal colon cDNA and KlenTaq polymerase (Clontech) as per manufacturers protocol. Products were then subcloned into the pCR2.1 plasmid vector (Invitrogen) and screened by PCR with internal primers for presence of the desired insert. Multiple RACE clones were subjected to DNA sequencing as described.

#### Example 5: Northern blot analysis

Northern blots containing the transfer yields of 2 µg poly A<sup>+</sup> RNA from a panel of normal tissues were obtained commercially (Clontech). Random primed <sup>32</sup>P labeled probes consisting of 300-600 bp PCR products from 5 prime coding sequences of serum positive cDNA clones were hybridized for 1.5 hours in Expresshyb (Clontech) at 68°C and washed at high stringency (2 times,

30 min. each, 0.1X SSC/0.1% SDS at 68°C). Resultant blots were used to expose Biomax MS autoradiography film (Eastman Kodak Co., Rochester, NY).

Table 4: Breast Cancer Associated Antigen Clone mRNA sizes

Clone	Size (kb)	Clone	Size (kb)	Clone	Size (kb)
LONY-Br-1	1.8	LONY-Br-17	1.0	LONY-Br-33	2.6
LONY-Br-2	2.9	LONY-Br-19	1.5	LONY-Br-34	2.1
LONY-Br-3	4.8	LONY-Br-20	2.4	LONY-Br-35	1.9
LONY-Br-4	1.2	LONY-Br-21	2.4	LONY-Br-36	0.8
LONY-Br-5	0.9	LONY-Br-22	1.6	LONY-Br-37	1.0
LONY-Br-6	1.4	LONY-Br-23	1.3	LONY-Br-38	2.2
LONY-Br-7	1.3	LONY-Br-24	3.9	LONY-Br-39	1.9
LONY-Br-8	0.9	LONY-Br-25	1.9	LONY-Br-40	3.4
LONY-Br-9	6.0	LONY-Br-26	1.5	LONY-Br-41	3.9
LONY-Br-10	3.6	LONY-Br-27	1.2	LONY-Br-42	0.6
LONY-Br-11	4.6	LONY-Br-28	0.5	LONY-Br-43	1.4
LONY-Br-12	2.2	LONY-Br-29	0.6	LONY-Br-44	0.7
LONY-Br-13	1.2	LONY-Br-30	0.8	LONY-Br-45	3.0
LONY-Br-14	0.8	LONY-Br-31	0.4	LONY-Br-46	3.7
LONY-Br-15	0.9	LONY-Br-32	2.2	LONY-Br-47	0.5
LONY-Br-16	2.5	LONY-Br-33	2.6	LONY-Br-48	1.6

#### Example 6: Isolation of gastric and prostate clones

A stomach cancer cDNA library was established, using standard techniques, then the library was screened, using the SEREX methodology described supra, and set forth by Sahin et al., *Proc. Natl. Acad. Sci. USA* 92: 11810 (1995), and by Chen et al., *Proc. Natl. Acad. Sci. USA* 94: 1914 (1997), incorporated by reference in their entirety.

To be specific, total RNA was isolated by homogenizing tumor samples in 4M guanidium thiocyanate/0.5% sodium N-lauryl sarcosine/ and 25 mM EDTA followed by centrifugation in 5.7 M CsCl/25 mM sodium acetate/10 uM EDTA at 320,000 rpm. Total mRNA was removed by passing the sample over an oligo-dT cellulose column. The cDNA libraries were then constructed

by taking 5 ug of mRNA, using standard methodologies to reverse transcribe the material.

Libraries were prepared from four different stomach cancer patients, referred to as "SM", "CK" and "SS" and "KM" respectively. A total of  $2.5 \times 10^6$ ,  $1.1 \times 10^6$ , and  $1.7 \times 10^6$  cDNA clones were obtained from the "SM", "CK" and "SS" individuals. Additional libraries were prepared from prostate cancer patient "OT".

The cDNA was used to construct a lambda phage library, and 500 phages were plated onto XL1-Blue MRF E. coli, and incubated for eight hours at 37°C. A nitrocellulose membrane was then placed on the plate, followed by overnight incubation. The membrane was then washed, four times, without TBS which contained 0.05% Tween, and was then immersed in TBS containing 5% non-fat dried milk. After one hour, the membrane was incubated with conjugates of peroxidase-goat anti human IgG specific for Fc portions of huma antibody (1:2000, diluted in TBS with 1% BSA. The incubation was carried out for one hour, at room temperature, and the membrane was then washed three times with TBS. Those clones which produced antibodies were visualized with 0.06%, 3,3'diamino benzidine tetrachloride, and 0.015%  $H_2O_2$ , in 50 mM Tris (pH 7.5). Any clones which produced immunoglobulin were marked, and then the membrane was washed, two further times, with TBS that contained 0.05% Tween, and then twice with "neat" TBS.

The membranes were then incubated in 1:100 diluted patient serum, overnight, at 4°C. The patient serum had been pretreated. Specifically, 5 ml samples were diluted to 10 ml with TBS containing 1% bovine serum albumin, and 0.02%  $Na_3N$ . The serum had been treated to remove antibodies to bacteriophage, by passing it through a 5 ml Sepharose column, to which a lysate of E. coli Y1090 had been attached, followed by passage over a second column which had E. coli lysate and lysate of E. coli infected with lambda bacteriophage. The screening was carried out five time. The samples were then diluted to 50 ml, and kept at -80°C, until used as described herein.

Following the overnight incubation with the membrane, the membrane was washed twice with TBS/0.05% Tween 20, and then once with TBS. A further incubation was carried out, using the protocols discussed supra, for the POD labelled antibodies.

The positive clones were then sequenced, using standard techniques. Following comparison of the sequences to information available in data banks, a total of 36 clones were resolved into known and unknown genes. In the table that follows, the "+" and "-" signs are essentially used to compare signals to each other. All were positive. Table 5, which follows, summarizes some of this

work isolation and sequencing of "SM" clones. Specifically, with reference to the first page of the table, previously identified human proteins and the nucleotide sequences, set forth in SEQ ID NOS:588-626 are known. The four molecules which follow in SEQ ID NOS:627-634 (gelsolin, zinc finger protein family, variant zinc finger motif protein goliath and homeodomain proteins), have not been identified in humans previously, although there are related molecules found in other species. Finally, with reference to Table 5, the last four moieties, i.e., prepro- $\alpha$  collagen, heterogeneous ribonucleoprotein D, nucleosome assembly protein 2, and NY-ESO-2/Ulsn NRP/V1 small nuclear ribonucleoprotein, are also known. Nucleotide sequences are set forth at SEQ ID NOS:635-642. The nucleic acid molecules having the nucleotide sequences set forth at SEQ ID NOS:643-670 represent molecules for which no related sequences were found. SEQ ID NO:671 combines the sequences of SEQ ID NOS:627-630, inclusive. SEQ ID NO:672 combines SEQ ID NOS:643-656, SEQ ID NO:673 combines SEQ ID NOS:657, 659 and 662, while SEQ ID NO:674 combines SEQ ID NOS: 658, 660, 661 and 663.

SEREX analysis of clones from libraries derived from patients "CK", "SS", "KM" (all gastric cancer) and patient "OT" (prostate cancer) was carried out as described above. The nucleotide sequences of clones derived from gastric cancer patients are presented as SEQ ID NOS:176-436. The nucleotide sequences of clones derived from prostate cancer patient "OT" are presented as SEQ ID Nos:437-543.

#### **Example 7: Isolation and analysis of colon clones**

Colon tumor samples were obtained as surgical samples, and were frozen at -80°C until ready for use.

Total RNA was then isolated from the samples, using the guanidium thiocyanate method of Chirgwin, et al., *Biochemistry* 18: 5294-5299 (1979), incorporated by reference. The total RNA thus obtained was then purified to isolate all poly A<sup>+</sup> RNA, using commercially available products designed for this purpose.

The poly A<sup>+</sup> RNA was then converted into cDNA, and ligated into  $\lambda$ ZAP, a commercially available expression vector, according to the manufacturer's suggested protocol.

Three cDNA libraries were constructed in this way, using colorectal carcinoma samples.

A fourth library, also from colorectal carcinoma, was prepared, albeit in a different way. The

fourth library was an IgG subtraction library, prepared by using a subtraction partner, generated by PCR amplification of a cDNA clone which encoded an IgG molecule. *See, e.g., Ace et al, Endocrinology* 134: 1305-1309 (1994), and incorporated by reference in its entirety. IgG subtraction is done to eliminate any false, positive signals resulting from interaction of cDNA clones which encode IgG, with the IgG then interacting with the anti-human IgG used in the SEREX assay, as described herein. PCR products were biotinylated, and hybridized with denatured second strand cDNA, at 68°C for 18 hours. Biotinylated hybrid molecules were coupled to streptavidin, and then removed by phenol chloroform extraction. Any remaining cDNA was also ligated into λZAP. All libraries were amplified, prior to immunoscreening.

Immunoscreening was carried out using sera obtained from patients undergoing routine diagnostic and therapeutic procedures. The sera were stored at -70°C prior to use. Upon thawing, the sera were diluted at 1:10 in Tris buffered saline (pH 7.5), and were then passed through Sepharose 4B columns. First, the sera were passed through columns which had *E. coli* Y1090 lysates coupled thereto, and then lysates from bacteriophage infected *E. coli* BNN97 lysates. Final serum dilutions were then prepared in 0.2% non-fat dried milk/Tris buffered saline.

The method of Sahin et al., *Proc. Natl. Acad. Sci. USA* 92:11810-11813 (1995), and U.S. Patent No. 5,698,396, both of which are incorporated by reference, was used, with some modifications. Specifically, recombinant phages at a concentration of  $4 \times 10^3$  phages per 15 cm plate (pfus), were amplified for six hours, after which they were transferred to nitrocellulose membranes for 15 hours. The membranes then were blocked with 5% nonfat dried milk.

As an alternative to the IgG subtraction procedure discussed above, membranes were prescreened in a 1:2000 dilution of peroxidase conjugated, Fc fragment specific goat anti-human IgG, for one hour, at room temperature. Color was developed using 3,3'-diaminobenzidine tetrahydrochloride, which permitted scoring of IgG encoding clones.

Membranes were then incubated in 1:100 dilutions of autologous sera, which had been pretreated with the Sepharose 4B columns, as described *supra*. The filters were then incubated, in a 1:3000 dilution of alkaline phosphatase conjugated Fc fragment specific, goat anti-human IgG, for one hour, at room temperature. The indicator system 4-nitroblue tetrazolium chloride/5-bromo-4-chloro-3-indolyl-phosphate was then added, and color development assessed. Any positive clones were subcloned, and retested, except the time on the nitrocellulose membrane was reduced to three

hours.

Positive clones were isolated and sequenced according to standard procedures. The nucleotide sequences of the clones are set forth in the even numbered sequences from SEQ ID Nos:544-586. The odd numbered sequences from SEQ ID Nos:545-587 represent the translated amino acid sequences of the colon nucleic acid clones. Analysis of probes for SEQ ID NOS:544 and 546 confirmed their universal expression.

The foregoing results reflect SEREX isolation of colon cancer clones using autologous serum. The positive clones were then rescreened, using allogeneic serum, following the same method discussed supra, in example 2, except IgG prescreening was omitted. The allogeneic sera was obtained from sixteen normal blood donors, and twenty nine patients who had been diagnosed with colorectal cancer.

The analysis with the two types of serum revealed that fourteen reacted with a subset of sera from normal and cancer patients, twenty-eight only with autologous sera, and six with both allogeneic and autologous sera. Over 60% of the allogeneic serum samples tested reacted with at least one of these positive clones. About 20% reacted with two or more.

In view of the results described above, further experiments were carried out using serum samples from patients with other forms of cancer, i.e., renal cancer (13 samples), lung cancer (23 samples), and breast cancer (10 samples). The results are set forth in Table 6 which follows:

Table 6: Allogeneic serotyping using colon cancer clones

Clone Number	Normal Sera	Colon Cancer	Renal Cancer	Lung Cancer	Breast Cancer
NY-Co-8	0/16	8/29	1/13	0/23	0/10
NY-Co-9	0/16	5/29	1/13	1/23	0/10
NY-Co-13	0/16	5/29	0/13	0/23	0/10
NY-Co-16	0/16	3/29	0/13	0/23	0/10
NY-Co-20	0/16	4/29	0/13	0/23	0/10
NY-Co-38	0/16	4/29	3/13	0/23	1/10

Of the six clones which were identified as being reactive with autologous and allogeneic

cancer serum, and not with normal serum, two were found to be identical to previously identified molecules (NY-Co-. Four others were found to have little or no homology to known sequences and thus are preferred allogeneic-reactive colon cancer clones. These nucleic acids and their polypeptide translations are presented as SEQ ID NOS: 544-551: SEQ ID NO: 544/545 (NY-CO-8), SEQ ID NO: 546/547 (NY-CO-9), SEQ ID NO: 548/549 (NY-CO-16) and SEQ ID NO: 550/551 (NY-CO-38). . Of twenty seven allogeneic colon cancer serum samples tested, 67% reacted with at least one of these antigens.

The expression pattern of mRNA corresponding to SEQ ID NOS:544, 546 and 550, as well as other sequences identified via the preceding examples was determined. To do this, RT-PCR was carried out on a panel of RNA samples, taken from normal tissue. The panel contained RNA of lung, testis, small intestine, colon, breast, liver and placenta tissues. The RNA was purchased from a commercial source. RNA from a colon tumor sample was also included. All samples were set up for duplicate runs, so that genomic DNA contamination could be accounted for. In the controls, no reverse transcriptase was used.

Primers were designed which were specific for the cDNA, which would amplify 5'-fragments, from 300-400 base pairs in length. The PCR reactions were undertaken at an annealing temperature of 68°C. Where appropriate, 5' and 3'-RACE reactions were undertaken, using gene specific primers, and adapter primers, together with commercially available reagents. Specifically, SEQ ID NOS: 546 and 550 were tested using RACE. The resulting products were subcloned into vector pCR 2.1, screened via PCR using internal primers, and then sequenced.

SEQ ID NOS:544 and 546 were found to be amplified in all tissues tested. SEQ ID NO:550 was found in colon tumor, colon metastasis, gastric cancer, renal cancer and colon cancer cell lines Colo 204 and HT29, as well as in normal colon, small intestine, brain, stomach, testis, pancreas, liver, lung, heart, fetal brain, mammary gland, bladder, adrenal gland tissues. It is was not found in normal uterine, skeletal muscle, peripheral blood lymphocytes, placental, spleen thymus, or esophagus tissue, nor in lung cancer.

The analysis also identified differential expression of a splice variant of SEQ ID NO:550, i.e., SEQ ID NO:552. When the two sequences were compared, it was found that SEQ ID NO:550 encodes a putative protein of 652 amino acids (SEQ ID NO:551), and molecular weight of 73,337 daltons. SEQ ID NO:552, in contrast, lacks an internal 74 base pairs, corresponding to



nucleotides 1307-1380 of SEQ ID NO:550. The deletion results in formation of a stop codon at the splice function, and a putative protein of 403 amino acids (SEQ ID NO:553), and molecular weight 45,839. The missing segment results in the putative protein lacking a PEST protein degradation sequence, thereby suggesting a longer half life for this protein.

5 In additional experiments, primers designed not to differentiate between SEQ ID NOS: 550 and 552 resulted in almost universal amplification (placenta being the only exception). In contrast, when primers specific for SEQ ID NO:552 were used differences were seen in normal pancreatic, liver, lung, heart, fetal brain, mammary gland, bladder, and adrenal gland tissue, where there was no expression of SEQ ID NO:552 found.

10 Northern blotting was also carried out for SEQ ID NOS: 544, 546, 550 and 552. These experiments employed the same commercially available RNA libraries discussed above were used.

Samples (2 ug) of polyA<sup>+</sup> RNA were analyzed from these samples, using random, <sup>32</sup>P labelled probes 300-360 nucleotides in length, obtained from PCR products. These probes were hybridized to the RNA, for 1.5 hours, at 68°C, followed by two washes at 0.1xSSC, 0.1% SDS, 15 68°C, for 30 minutes each time.

SEQ ID NOS:544 and 546 were again found to be universally expressed.

Further screening identified additional isoforms of SEQ ID NOS:544 and 550. These are set forth as SEQ ID NOS: 554, 556, 558 and 560. The isoform represented by SEQ ID NO:554 (translated as SEQ ID NO:555) is a naturally occurring splice variant of SEQ ID NO:544, found 20 in normal colon. SEQ ID NO:556 (translated as SEQ ID NO:557), which is an isoform of SEQ ID NO:550 (translated as SEQ ID NO:551), was found in brain tissue, primarily spinal chord and medulla. SEQ ID NO:558 (translated as SEQ ID NO:559), was found in normal kidney and in colon tumors, metastasized colon cancer, renal cancer, gastric cancer, and in colon cancer cell line Colo 205. It was not found in any normal tissue other than kidney.

25 The nucleic acid molecule whose nucleotide sequence set forth as SEQ ID NO:560 (translated as SEQ ID NO:561), is a further isoform of SEQ ID NO:552. It is similar to SEQ ID NO:558, except it contains a long nucleotide insert encoding a longer COOH terminus. It was expressed in normal bladder and kidney cells, and renal cancer cells. It was not expressed in colon cancer cells.

30 It is reported above that fourteen clones reacted with subsets of serum from both normal

and cancer patients, while twenty eight reacted with autologous sera only. These clones were sequenced, in accordance with standard, art recognized methods. Of the clones which reacted only with autologous sera, nine appear to be previously unidentified sequences. These are set forth as SEQ ID NOS: 562, 564, 566, 568, 570, 572, 574, 576 and 578. SEQ ID NO:562 (translated as SEQ ID NO:563) is 1445 nucleotides long, and shows some similarity to known sequences for myosin and tropomyosin. SEQ ID NO:564 (translated as SEQ ID NO:565), which is 1226 nucleotides long, contains a TPR motif. The sequence set forth in SEQ ID NO:566 (translated as SEQ ID NO:567) is 1857 nucleotides long, and shows similarity to cyclophilins. The nucleotide sequence set forth in SEQ ID NO:568 (translated as SEQ ID NO:569) is 1537 nucleotides long, and shows similarity to murine gene 22A3, which has unknown function, but resembles an unconventional form of myosin, as well as an EST for heat shock inducible mRNA. As for the molecule set forth in SEQ ID NO:570 (translated as SEQ ID NO:571), it appears to resemble a nucleic targeting signal protein. SEQ ID NO: 572 (translated as SEQ ID NO:573) is 604 nucleotides long, and may encode a lysosomal protein. The molecule set forth in SEQ ID NO:574 (translated as SEQ ID NO:575) is 742 nucleotides long, and encodes a protein with an SH3 domain and which shows some similarity to GRB2 and human neutrophil oxidase factor. The molecule set forth in SEQ ID NO:576 (translated as SEQ ID NO:577) is 1087 nucleotides long, and encodes a protein which contains coiled core domains. The molecule set forth in SEQ ID NO:578 (translated as SEQ ID NO:579) is 2569 nucleotides long, shows some similarity with *Drosophila* homeotic material tudor protein, and has a DY(F)GN repeat.

Additional sequences were identified which were expressed in both normal sera and cancer cells. The sequence set forth in SEQ ID NO:580 (translated as SEQ ID NO:581), e.g., is 2077 nucleotides long, and was expressed by both colorectal cancer and normal cells. Analysis of the sequence showed that it possesses a nuclear targeting sequence. The molecule set forth in SEQ ID NO:582 (translated as SEQ ID NO:583) is 3309 nucleotides long, was expressed by colorectal cancer and normal cells, and is similar to heat shock protein 110 family members. The molecule presented in SEQ ID NO:584 (translated as SEQ ID NO:585) was expressed in a colon to lung metastasis, as well as by normal tissue. It is 2918 nucleotides in length. Analysis shows that it contains 2 zinc finger domains. The nucleotide sequence of SEQ ID NO:586 (translated as SEQ ID NO:587) was also expressed in a colon to lung metastasis, is 1898 nucleotides long, and is

also expressed by normal tissue. Specifically, the reactivity of the molecules was as follows:

Table 7

5	SEQ ID NO:	Normal Sera Reactivity	Tumor Sera Reactivity
	580	2/16	2/16
	582	2/16	3/16
10	584	2/16	2/16
	586	2/8	1/16

A more extensive set of RT-PCR experiments were carried out to study the expression pattern of SEQ ID NOS: 550, 552, 558 and 560. The results follow.

Table 8: RT-PCR analysis of colon SEREX clones

	<u>normal tissue</u>	<u>SEQ ID NO.:550</u>	<u>SEQ ID NO.:552</u>	<u>SEQ ID NO.:558</u>	<u>SEQ ID NO.:560</u>
20	kidney	+	Negative	Negative	Negative
	colon	+	Negative	Negative	Negative
	small		Negative	Negative	Negative
	intest.	+	Negative	Negative	Negative
	brain	+	Negative	Negative	Negative
25	stomach	+	Negative	Negative	Negative
	testis	+	Negative	Negative	Negative
	pancreas	+	Negative	Negative	Negative
	lung	+	Negative	Negative	Negative
	liver	+	Negative	Negative	Negative
30	heart	+	Negative	Negative	Negative
	fetal		Negative	Negative	Negative
	brain	+	Negative	Negative	Negative
	mammary		Negative	Negative	Negative
	gland	+	Negative	Negative	Negative
35	bladder	+	Negative	Negative	Negative
	adrenal		Negative	Negative	Negative
	gland	+	Negative	Negative	Negative
	uterus	Negative	Negative	Negative	Negative
	skeletal		Negative	Negative	Negative
40	muscle	Negative	Negative	Negative	Negative
	PBL	Negative	Negative	Negative	Negative
	placenta	Negative	Negative	Negative	Negative

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	spleen	Negative	Negative	Negative	Negative
	thymus	Negative	Negative	Negative	Negative
	esophagus	Negative	Negative	Negative	Negative
	<u>Tumor Tissue</u>				
5	renal				
	cancer (4)	+ (2/4)	+ (2/4)	+ (2/4)	+ (2/4)
	colon				
	primary				
	tumors (10)	+ (10/10)	+ (10/10)	+ (10/10)	Negative
10	colon				
	mets (4)	+ (4/4)	+ (4/4)	+ (4/4)	Negative
	breast				
	cancer (6)	+ (3/6)	Negative	Negative	Negative
	lung				
15	cancer (6)	+ (6/6)	Negative	Negative	Negative
	gastric cancer (1)	+	+	+	Not tested
	<u>colon cancer cell lines</u>				
	colo 205	+	+	+	Negative
	HT29	+	+	Negative	Negative
20	HCT15	Negative	Negative	Negative	Negative

**Example 8: Isolation and analysis of additional clones**

For the establishment of a cDNA library from human tissue total RNA was obtained from 0.5 g of a renal clear cell carcinoma and established according to the method of Chomzynski as described above. The mRNA was extracted from total RNA with oligo-dT-cellulose. The synthesis of the first strand cDNA was accomplished by the method described by Gubler and Hoffmann, *Gene* 25: 263 (1983) using RNase H and DNA polymerase I. For adaptation of the cDNA Klenow enzyme, adaptors with EcoRI restriction enzyme sites were ligated to the cDNA ends using T4 DNA ligase (Ferretti L and Sgamerella V, *Nucl. Acids Res.* 9: 3695 (1981)). Following restriction enzymatic digestion with the enzyme XhoI, cDNA molecules of different length were separated using Sephacryl 400 and transfected into  $\lambda$ ZAPII phage vectors (Short JM et al., *Nucleic Acids Res.* 16: 7583 (1988)). The recombinant phage DNA was packaged into phages after ligation with packaging extracts and used for the transfection of *E. coli* bacteria. The titration of the library resulted in  $1.8 \times 10^6$  recombinant primary clones. The total cDNA library was transfected in *E. coli* and amplified. The titer of the cDNA library after amplification was  $10^{11}$  plaque forming units per ml (pfu/ml). These transfected cells were used in experiments which follow.

In accordance with the invention as described above, identification of immunogenic material was achieved by using human sera which has been completely depleted of antibodies directed against antigens derived from native and lytic  $\lambda$  phage-transfected *E. coli* bacteria. To this end, the serum was absorbed, as follows.

5 *E. coli* bacteria of the strain XL1-blue were cultured in 50 ml LB medium overnight. After achieving an optical density of  $OD_{600} = 1.0$ , the bacteria were pelleted by centrifugation, resuspended in 5 ml phosphate buffered saline (PBS), and lysed by sonication. The bacterial lysate was bound onto a matrix of activated Sepharose, which was then put into a column and used for the absorption of the human serum. The serum was run over this column 10 times.

10 A culture of *E. coli* XL1 blue bacteria in the exponential growth phase was pelleted by centrifugation, transfected in 0.01 M magnesium sulfate with  $10^6$   $\lambda$ ZAPII phages without a recombinant insert and incubated in 5 ml LB medium for four hours. The lysate of the transfected bacteria was used in the same manner as the untransfected bacteria, with the human serum described supra being passed through the column an addition ten times.

15 To complete the depletion of the serum, interfering antibodies from lytically transfected *E. coli* bacteria were cultured on agar plates and their proteins were blotted onto nitrocellulose membranes after 10 hours of culture at 37°C. Following this, the serum which had been preabsorbed according to the above steps was transferred to the blotted nitrocellulose membrane, and the absorption procedure was repeated five times. The serum, which was processed in  
20 accordance with the invention, was totally depleted of antibodies directed against antigens derived from *E. coli* and phages.

In this, a renal cancer-specific antigen was identified via the following steps. Bacteria of the strain XL1 blue were transfected with recombinant phages derived from the described cDNA library and plated at a density of  $4-5 \times 10^3$  plaque forming units (pfu) per plate in LB-medium with  
25 isopropylthiogalactopyranoside ("IPTG"). After 12 hours of incubation at 37°C, nitrocellulose membranes were put on top of the cultures and culture plates were incubated for another four hours. This was followed by incubation of the nitrocellulose membrane for one hour in Tris-buffered saline (PBS) with 5% milk powder. After washing the nitrocellulose membranes three times in TBS, the stripped human serum secured following Example 2 was diluted 1:1000 in TBS/0.5% (w/v) milk  
30 power and incubated overnight with gentle shaking. After the incubation with the nitrocellulose

membrane the serum was removed and kept for additional testing. Following incubation with serum, the nitrocellulose membranes were washed three times in TBS, and incubated with a polyclonal alkaline phosphatase-conjugated goat anti-human IgG serum for one hour. Following this, the nitrocellulose membranes were washed repeatedly with TBS/0.01% (v/v Tween 20). The reaction was developed using nitroblue tetrazolium chloride and bromochloro-indoyl-phosphate in TBS. The binding of human antibodies to the expressed protein became visible by a blue ring-formed color deposit on the nitro-cellulose membrane. The efficient preabsorption of the serum made it possible to develop the membrane at 37°C over several hours without compromising the quality of the test because of background reactivity caused by antibodies against *E. coli* and phage antigens.

Positive clones were localized on the agar plates, transferred into transfection buffer, and used for a second round of transfection and subcloning. A total of  $1.8 \times 10^6$  recombinant clones were subjected to screening and five different positive-reacting clones were identified.

Positive clones, i.e., those which had bound antibodies derived from the processed human serum, were subcloned to monoclonality by repeated rounds of transfection and testing of reactivity with the processed human serum. P-bluescript phagemids with the respective cDNA inserts were cloned by *in vivo* excision (Hay B and Short JM, *Strategies* 5: 16-19, 1992) from the  $\lambda$ ZAPII phage vectors and used for the transfection of *E. coli* SOLR bacteria. Plasmids were isolated from the bacteria after alkaline lysis with NaOH in a modification of the method of Birnboim HC and Doly J. *J. Nucl. Acids Res.* 7: 1513 (1979). The recombinant plasmid DNA was sequenced according to standard methods using M13-forward and M13-reverse oligonucleotides. The DNA sequence obtained and the resulting amino acid sequence were compared with nucleic acid and protein data banks (Gene Bank, EMBL, Swiss Prot). The sequencing of the cDNA inserts was continued using internal oligonucleotides. Analysis showed no homology with any sequences deposited in the data banks. The full length cDNA clone, referred to as SK313, was cloned with the RACE method (Frohman MA, Dush MK, Martin GR, *Proc. Natl. Acad Sci. USA* 85: 8998 (1988)), and had a carbonic anhydrase domain at the 5' end.

As a continuation of these experiments, RNA was isolated from a spectrum of malignant and normal human tissues and Northern blots were performed with labeled SK313 (also referred to as clone HOM-RCC-313). The Northern blot analysis demonstrated that the mRNA of clone HOM-

RCC-313 was overexpressed in 4 out of 19 renal cell carcinomas compared to normal kidneys. Very weak expression was found only in colonic mucosal tissue and in normal kidney. Expression in other tissues was not observed.

To determine the incidence of antibodies against antigens which are identified above, 5 allogeneic sera from healthy individuals and tumor patients were analyzed. To this end, the sera were processed as described above and depleted from antibodies against antigens derived from *E. coli* and phages. For the detection of antigen-specific antibodies, phages derived from reactive clones were mixed with non-reactive phages derived from the same cDNA library at a ratio of 1:10 and tested as described above for reactivity with antibodies in the human test serum. The serum 10 which had been used for the identification of the antigen was used as a positive control. The non-reactive phages served as a negative control. A serum sample was positive for antigen reactive antibodies, if the expected percentage of the phage plaques showed a positive reaction. In the case of the renal cell carcinoma antigen represented by clone HOM-RCC-313, the analysis of a spectrum of human sera showed that only sera from renal cell carcinoma patients contained reactive 15 antibodies. Sera from healthy controls and patients with other tumors did not contain such antibodies.

The cDNA for clone HOM-RCC-313 was excised from the plasmid DNA by digestion with the restriction enzyme *EcoR*I, was separated by agarose gel electrophoresis, followed by extraction from the gel. This was then used to create a vector which expresses a fusion protein with the 20 bacterial protein anthranilate synthetase. A relevant fragment in the exact open reading frame was cloned into pATH plasmid vectors (Koerner et al., *Meth. Enzymol.* 194: 477 (1991)). Induction of protein expression was obtained after transformation of the plasmids into *E. coli* of strain BL21 as described (Spindler et al., *J. Virol.* 49: 132 (1984)). Expressed fusion proteins were separated by SDS gel electrophoresis, excised from the gel, eluted and freeze dried. Rabbits were immunized by 25 subcutaneous injection with 100 µg of the lyophilisate combined with Freund's adjuvant according to standard procedures. Immunization was repeated three times at two-week intervals using incomplete Freund's adjuvant. The rabbit was bled and antiserum was obtained. The obtained antiserum was depleted from antibodies reactive with *E. coli* and phages as described above and tested for reactivity against the renal carcinoma antigen as described for the human serum. 30 Reactivity was detected at dilutions of 1: >100,000.

Additional clones were identified from pancreatic cancer tumor specimen using the SEREX method of Sahin et al., (1995). A cDNA library was prepared and reacted with high titer IgG in sera of pancreatic carcinoma patients. A total of  $8 \times 10^5$  clones were screened with autologous serum, and  $4.5 \times 10^3$  clones were screened with three different allogeneic sera. Twenty three clones, representing  
5 seven different transcripts were found. Four were previously unknown, unisolated genes. Of the remaining three, glycolytic enzyme aldolase A was found (SEQ ID Nos:799 and 800). Another molecule was "known" in that it was homologous to the rat eIF-5 gene (SEQ ID Nos:801 and 802), which is a eukaryotic translation initiation factor. The human eIF-5 gene was not previously known.

When hepatocellular carcinoma libraries were studied in the same way, a total of  $1.5 \times 10^6$   
10 clones were screened, and 98 positives were found. A total of 59 of these were sequenced, and corresponded to at least 20 different transcripts. Nine of these were assayed with allogeneic sera from hepatocellular cancer (HCC) patients and normal patients. High titered antibody was restricted to HCC patients. The majority of isolated sequences did not correspond to known molecules. Three  
15 which did were human albumin (SEQ ID Nos:803 and 804), senescence marker protein SMP30 (SEQ ID NOs:805 and 806), and C3VS (SEQ ID NOs:807 and 808). The latter was overexpressed in 2 of 4 hepatocarcinoma tissues, as compared to normal. Expression of SMP30 was found to vary highly.

The methodology was combined with subtractive cDNA techniques when assaying leukemia cells (T-ALL). An antigen was found which was identical to a broadly expressed, DNA repair  
20 enzyme.

Further assays identified the known molecule galectin-9 (SEQ ID NOs:809 and 810), as being highly expressed on human macrophages and dendritic cells. Expression is upregulated during differentiation of monocytes to macrophages. Highest levels were found on monocyte derived, dendritic cells.

25 Fusion proteins "LD1-mFc" and "LD2-mFc" were constructed to help analyze galectin-9. These consist of murine IgG heavy chain fragments, and a lectin domain (LD1, or LD2), as the N-terminus. Analysis indicated that the C-terminal lectin domain binds to the surface ligands, while the cell surface ligands recognized by the C-terminal lectin domain of galactin-9 was expressed only in a small, subpopulation of dendritic cells.

30 Further analysis of ovarian cancer cells (500,000 clones, using the SEREX method described



above), identified previously known antigens MAGE-4 (SEQ ID Nos:811 and 812) and restin (SEQ ID Nos:813 and 814), and six other newly identified molecules.

Further experiments were carried out which involved restin. A variation of restin is known, i.e., "CLIP170", which was reported to mediate binding of endosomes to microlubules. It was found that both resin and CLIP 170 are highly expressed in dendritic cells, and are involved in the formation and transport of macropinosomes, a feature of professional antigen presenting cells. Expression of restin was induced after 48 hours of culture of monocytes in GM-CSF/IL-4 supplemented medium. Highest levels were found in immature dendritic cells. When microlubile systems, which are essential for the activity of restin/CLIP-170 were disrupted, macropinocytosis was lost completely.

Further work with the methodology disclosed herein on glioma identified a clone encoding nm23-H2 protein (SEQ ID Nos:815 and 816). This clone corresponds to subunit B of nucleoside diphosphate kinase, which is implicated in tumor metastasis control. It is also known as PuF, a transcriptional factor, for c-myc proto-oncogenes. Antibodies against the protein were found in 1 of 18 sera of brain malignancy patients, 3 of 20 melanoma patients, and 2 of 20 sera from healthy patients. When expression studies were carried out using RT-PCR, 25 of 28 brain tumor, and 4 or 5 meningioma tumor samples were found to express the gene.

#### **Example 9:Isolation and analysis of lung cancer clones**

A cDNA library was constructed from a case of moderately differentiated adenocarcinoma of the lung, obtained from the Department of Pathology at The New York Hospital. The library was constructed in a  $\lambda$ ZAP Express vector using a cDNA library kit (Stratagene, La Jolla, CA).

The cDNA library was screened with autologous patient's serum as described previously [Sahin, U. et al., *Proc Natl Acad Sci USA* 92:11810-3 (1995); Chen, Y.T. et al. *Proc Natl Acad Sci USA*. 94:1914-8 (1997)]. Briefly, the serum was diluted 1:10, pre-absorbed with transfected *E. coli* lysate, and a 1:10 dilution of the absorbed serum (final dilution of serum 1:100) was incubated overnight at room temperature with the nitrocellulose membranes containing the phage plaques. After washing, the filters were incubated with alkaline phosphatase-conjugated goat anti-human Fc  $\gamma$  secondary antibodies and the reactive phage plaques were visualized by incubating with 5-bromo-4-chloro-3-indolyl-phosphate and nitroblue tetrazolium. Phagemid clones encoding human

immunoglobulin sequences were subsequently eliminated during the secondary screening.

The reactive clones were subcloned, purified, and *in vitro* excised to pBK-CMV plasmid forms (Stratagene). Plasmid DNA was prepared using Wizard Miniprep DNA Purification System (Promega, Madison, WI). The inserted DNA was evaluated by EcoRI-XbaI restriction mapping, and clones representing different cDNA inserts were sequenced. The sequencing reactions were performed by DNA Services at Cornell University (Ithaca, NY) using ABI PRISM (Perkin Elmer) automated sequencers.

To evaluate the mRNA expression pattern of the cloned cDNA in normal and malignant tissues, gene-specific oligonucleotide primers for PCR were designed to amplify cDNA segments of 300-400bp in length, with the estimated primer melting temperature in the range of 65-70°C. All primers were commercially synthesized (Operon Technologies, Alameda, CA). RT-PCR were performed using 35 amplification cycles in a thermal cycler (Perkin Elmer) at an annealing temperature of 60°C.

Genomic DNA were extracted from cell lines and frozen tumor tissue. Following restriction enzyme digestion, the DNA was separated on a 0.7% agarose gel, blotted onto nitrocellulose filters, and hybridized to an a <sup>32</sup>P-labeled DNA probe at high stringency (65°C, aqueous buffer). Washing of the blot was also under high stringency conditions, with a final wash in 0.2XSSC with 0.2% SDS at 65°C.

To identify the 5' end of the mRNA transcripts, RACE (rapid amplification of cDNA ends) methodology was utilized using the Marathon cDNA amplification kit (Clontech) and adaptor-ligated testicular cDNA as the substrate. The PCR products, after separation by agarose gel electrophoresis, were cloned into the direct PCR cloning vector pGEM-T (Promega).

Single-strand conformation polymorphism (SSCP) analysis was performed to analyze cDNA from various tissues, using previously described protocols [Dracopoli, C.D. et al., New York: John Wiley and Sons, Inc. (1997)]. Briefly, PCR was performed with 5 µl RT product in a final volume of 25 µl, with 2µCi of α<sup>32</sup>P-dCTP (~3000 Ci/mmol, New England Nuclear) per reaction. The PCR conditions was as described for RT-PCR above. After the PCR, 1 µl of the mixture was diluted with 5 µl of denaturing buffer (95% formamide, 20 mM EDTA, 0.05% bromophenol blue, 0.05% xylene cyanol), heat-denatured at 98°C for 2 min, and electrophoresed through an 8% polyacrylamide gel with 10% glycerol. As controls, aliquots of the same samples were diluted with a standard non-

denaturing DNA loading dye and electrophoresed in parallel. The electrophoresis was performed at room temperature at a constant power of 10-12 watts. The gel was then dried and autoradiography performed for 15-24 hours with an intensifying screen.

#### 5 Identification of Immunoreactive cDNA clones

A cDNA expression library of  $1.42 \times 10^7$  primary clones was prepared from Lu15, a specimen of moderately differentiated adenocarcinoma of the lung and  $8 \times 10^5$  phage plaques were immunoscreened with absorbed autologous patient serum at 1:100 dilution. Excluding false-positive clones encoding immunoglobulin gene fragments, 20 positive clones were identified. These clones were purified and sequence analyzed. Comparisons of the sequences showed that these clones represented cDNAs from 12 distinct genes, designated NY-LU-1 through NY-LU-12 (Table 9). A homology search through the GenBank/EMBO databases revealed that 4 of the 12 genes corresponded to previously known molecules, and 8 others were unknown genes, with sequence identity limited only to short segments of known genes or to expressed sequence tags (ESTs).

15 Table 9: NY-LU clones

Gene Designation	Gene/Sequence Identity [Accession Number]	cDNA	Comments
NY-LU-1	Aldolase A (N and H type) [X06352]	Lu-15/24, 72, 83, 158, 219, 241	Human fructose, 1,6 diphosphate aldolase A. Expressed in muscle (M type), but also in most other tissues (N and H types). Levels increased in most lung cancers; released into blood upon trauma and in several cancers.
NY-LU-2	hASNA-1 [U60276]	Lu-15/26, 66	Human homolog of the ATP-binding ars A component of the bacterial arsenite transporter. Previously cloned by SEREX from a testicular library (Chen et al., unpolished). Ubiquitously expressed.
NY-LU-3	Annexin 1X [L19605]	LU-15/64	Homosapiens 56K autoantigen. Antibodies to Annexin 1X are found in multiple autoimmune diseases. ubiquitously expressed.

NY-LU-4	Rip-1 [U55766]	Lu-15/65	Human HIV Rev-interacting protein. Expressed in B cells, monocytes and rhabdomyoma cells.
NY-LU-5	Unknown [W61291, W92962, etc.]	Lu-15/80	Expressed ubiquitously (by RT-PCR).
NY-LU-6	Unknown [none]	Lu-15/85	Sequence contains no ORF, expressed ubiquitously (by RT-PCR).
NY-LU-7	Unknown [W23466, AA167732, etc.]	Lu-15/135,217	Expressed in neuron, pregnant uterus, lung ca., parathyroid tumors, etc.
NY-LU-8	Unknown [Z78323, N39225, etc.]	Lu-15/139	Expressed in fetal heart, retin, multiple sclerosis, etc.
NY-LU-9	Unknown [W26569, AA036884, etc.]	Lu-15/145	Expressed in retina, pregnant uterus, fetal liver-spleen, etc.
NY-LU-10	Unknown [M29204, etc.]	Lu-15/154	Expressed in colon, pancreas, pregnant uterus, fibroblasts, etc.
NY-LU-11	Unknown [W23466, AA057400, etc.]	Lu-15/270	Expressed in retina, pregnant uterus, fetal heart, fetal liver-spleen, parathyroid tumors, etc.
NY-LU-12	g16	Lu-15/251	Located at the 3p21 TSG locus (see text)

Of the 4 known genes, aldolase A (NY-LU-1; SEQ ID NOs:689 and 690) was most frequently isolated, representing 6 of 20 primary positive clones in the entire screening. NY-LU-2 (SEQ ID NO:691), represented by two isolates, was the human homolog of the ATP-binding *arsA* component of the bacterial arsenite transporter, a gene which has been shown to be ubiquitously expressed in various tissues [Kurdi-Haidar, B. et al., *Genomics* 36:486-91 (1996)]. NY-LU-3 (SEQ ID Nos:692 and 693) encodes annexin XI, which is a 56KD ubiquitously expressed antigen to which autoantibodies have been described in sera from patients with various autoimmune diseases [Misaki, Y. et al., *J Biol Chem* 269:4240-6 (1994); Misaki, Y. et al., *J Rheumatol.* 22:97-102 (1995)]. The last gene in this group, NY-LU-4 (SEQ ID NOs:694 and 695), codes for the human HIV Rev interacting protein Rip-1, which has been shown to be expressed in the monocyte cell line U937, the rhabdomyoma cell line RD, as well as in adherent monocytes and primary lymphocytes [Refaeli, Y.

et al., *Proc Natl Acad Sci USA* 92:3621-5 (1995)].

Of the eight unknown genes, 6 (NY-LU-5, 7, 8, 9, 10, 11; SEQ ID Nos:696, 698, 699, 700, 701 and 702/703, respectively) shared sequence identify with reported expressed sequence tags (EST), likely representing cDNA products derived from the same genes. These ESTs were derived from various somatic tissues unrelated to lung, e.g., neuron, pregnant uterus, colon, endothelial cells, etc., suggesting that these genes are widely expressed in human tissues (Table 9), making them unlikely candidates for vaccine-based tumor immunotherapy. These clones were not further investigated. The only novel gene in this group, NY-LU-6 (SEQ ID NO:697), showed no sequence identity to deposited sequences in the public databases. The tissue expression pattern of this gene was evaluated by RT-PCR analysis using gene-specific primers and a normal tissue RNA panel consisting of lung, colon, kidney, liver, brain and testis. Results showed universal expression in these tissues, and this clone was not further analyzed.

NY-LU-12 is on TSG locus of chromosome 3p21.

The last gene in the unknown gene group, NY-LU-12, was represented by the immunoreactive clone Lu15-251. This clone, 1081bp in length, contained an uninterrupted open reading frame (ORF) of 952 bp, followed by a 129bp 3'untranslated region. No translation initiation codon was identified, indicating that this was a partial cDNA clone.

A sequence homology search revealed that this gene shared up to 30% homology with two different human proteins at its C-terminus (Fig. 1), LUCA15 and DXS8237E (GenBank accession numbers U23946, and P98175) and also shared homology to S1-1, the rat counterpart of DXS8237E [Inoue, A. et al., *Nucleic Acids Res.* 24:2990-7 (1996)]. LUCA15 was subsequently proven to be a gene immediately centromeric to NY-LU-12 on the TSG locus on chromosome 3p21 (see below and [Wei, M.H. et al., *Cancer Res.* 56: 2487-92 (1996)]). Our analysis of LUCA15 revealed the presence of a nuclear localization signal in the putative LUCA15 protein. DXS8237E, was located on chromosome Xp11.23 [Coleman, M.P. et al., *Genomics* 31:135-8 (1996)] and its rat homolog, S1-1, has been shown to be an RNA-binding protein [Inoue, A. et al., *Nucleic Acids Res.* 24:2990-7 (1996)].

Of particular interest, however, was that a short segment (92bp) at the 5' end of NY-LU-12 was identical to a previously identified gene, g16 (GenBank accession number U50839), which was

mapped to chromosome 3p21.3 and was interrupted in the small cell lung cancer line NCI-H740.

To compare NY-LU-12 with g16, the full-length NY-LU-12 cDNA sequence was obtained from normal testicular mRNA through a combination of 5'RACE and direct PCR cloning strategies. The predominant cDNA form (SEQ ID No:707), excluding the poly A tail, is of 3591bp in length.

5 An open-reading-frame of 1123 amino acid residues (SEQ ID No:708) was identified (nt. 102-3470), with 101bp of 5' untranslated and 129bp of the 3' untranslated region. The nucleotide and amino acid sequences are shown in Fig. 2.

Comparison with the g16 sequence verified that these two are identical genes and mapped NY-LU-12 to *TSG* locus on 3p21. However, the reported g16 sequence, 2433 bp in length, lacks the  
10 5' end 110 bases which include the translational initiation codon at nucleotide 102, and also the 3' end 980 nucleotides of NY-LU-12. In addition, 74bp DNA segment (nt. 1587-1659 of NY-LU-12) was absent in the reported g16 sequence. Oligonucleotide primers flanking this 74 bp region were designed and used to amplify RNA from 1 normal lung, 5 lung cancer cell lines, and 6 lung cancer specimens. Two RT-PCR products were seen in every specimen, corresponding to the sizes of the  
15 two cDNA variants. It was thus concluded that this variation represents an alternate splicing event which occurs in both normal and cancerous lung tissues. Of interest, however, was the difference in the putative translational products resulting from this additional 74bp exon. In the absence of this exon, the open-reading-frame of NY-LU-12 would end in the termination codon at nt.1736, as reported for g16, with a total length of 520 amino acid residues (in contrast to 1123 residues in the  
20 longer transcript). Moreover, this shorter form would not encode the C-terminal portion of the NY-LU-12 protein, the segment responsible for the immunoreactivity of Lu15-251 to the autologous patient serum.

#### Additional cDNA variants of NY-LU-12

25 In the process of 5'RACE cloning of the full-length NY-LU-12, three minor forms of cDNA products were identified which varied in their transcriptional initiation site and in their exon usage in the 5' segment of this gene. These variants will be described as transcripts B, C, and D (SEQ ID Nos:709, 711 and 712). Fig. 3 shows the comparison of these transcripts to the predominant cDNA form (transcript A, see Fig. 2).

30 Transcript B (Fig. 3A, bottom) contains an additional exon of 208 base pairs, inserted at

nucleotide 145 of the NY-LU-12 sequence. The original ORF of NY-LU-12 is disrupted due to this inserted sequence, and the AUG initiation codon used by transcript A is thus unlikely to be used by this transcript. A new potential translational initiation site, however, is found within this new exon and would continue the translation into the ORF of transcript A. The final product would be a protein of 1177 amino acids (SEQ ID NO:710), with the 69 residues at the N-terminus different from transcript A. Interestingly, this new exon encodes for a signal peptide not present in the transcript A (Fig. 3A, bottom), and it is possible that these two products are localized to different subcellular compartments.

Similar to transcript B, transcripts C and D both contained additional exon(s) not present in transcript A. Transcript C contained two extra exons in tandem and a length of 364bp, only one of which (137bp) was present in transcript D, Figure 3B. These extra exon(s), inserted at the same alternate splicing site as transcript B, disrupted the original ORF, and the only long ORF would initiate at nucleotide position 498 of NY-LU-12 (959 of transcript C, 635 of transcript D). Considering the long untranslated region at the 5' end, it is doubtful whether transcripts C and D are indeed translated *in vivo*.

Correlating with this variation of NY-LU-12 mRNA, Northern blot analysis showed several RNA species in normal tissues, ranging approximately from 3 to 4.4 Kb. The intensity of individual bands also appear to vary among different tissues, suggesting post-transcriptional tissue specific regulation of NY-LU-12 mRNA.

#### Features of NY-LU-12 and its putative gene product

Analysis of the NY-LU-12 amino acid sequence showed 20 inexact 6 amino acid repeats with a consensus sequence of D(F/Y)RGR(D/E) close to the N-terminus (Fig. 2). These repeats were separated by 4 to 6 amino acid intervals, which showed no apparent sequence homology among each other. This feature in primary sequence is distinctive among known proteins. Hydrophilicity plot revealed that this region, although hydrophilic in general, has regular hydrophobic turns, and these cycles of hydrophilicity changes correspond to the hexapeptide repeats. Although the significance of this characteristic is unclear at present, this segment of sequence is highly rich in arginine and aspartic acid, a feature shared by RNA binding proteins. Similar motifs, rich in arginine and aspartic acid residues, were found in other RNA-binding proteins [Witte, M.M.

et al., *Proc Natl Acad Sci USA* 94: 1212-7 (1997); Wilson, R. et al., *Nature* 368:32-8 (1994); Seraphin, B. et al., *Nature* 337:84-7 (1989); Takagaki, Y. et al., *Proc Natl Acad Sci USA* 89:1403-7 (1992)], e.g., RNA [Seraphin, B. et al., *Nature* 337:84-7 (1989)] hnRNA 3' end cleavage stimulation factor [Takagaki, Y. et al., *Proc Natl Acad Sci USA* 89:1403-7 (1992)], etc., indicating that NY-LU-12 is likely to be an RNA-binding protein. Consistent with this, PROSITE analysis of the putative NY-LU-12 protein identified a bipartite nuclear localization signal between amino acids 1016-1032 and a 4-residue nuclear localization pattern (PRKR) at amino acid 604-607 (Fig. 2), suggesting that NY-LU-12 is a nuclear protein. Analysis for post-translational modification sites showed potential sites for tyrosine sulfation, amidation, as well as phosphorylation sites for protein kinase A, C, casein kinase II, and tyrosine kinase. A PEST region, peptide sequences consistently found among unstable proteins with short half lives, was identified at amino acids 897-928 (Fig. 2), implying NY-LU-12 as an unstable protein.

#### Southern blot analysis of NY-LU-12 in normal and tumor tissues

To investigate the status of NY-LU-12 in normal and tumor cells, Southern blot analysis was performed on 9 lung cancer cell lines (3 adenocarcinoma, 2 squamous, and 3 large cell anaplastic), Lu15 tumor DNA, and a colon cancer cell line HT29 (Fig. 4). (HT29 was included due to the finding of an EST identified in the GenBank, accession number AA079461, which appeared to be a fusion sequence between semaphorin IV gene and NY-LU-12.) Using a 1.1Kb cDNA probe (nucleotide 1095-2140) and HindIII digested DNA, the results showed that one of the two hybridizing bands was absent in NCI-H740, confirming that NY-LU-12 was partially deleted in this cell line. The breakpoint of this deletion, by using primers from different regions, was further defined to be between nucleotides 1433 and 1777 of NY-LU-12, with the 3' sequences homozygously deleted. Besides NCI-H740, however, no evidence of homozygous deletion was seen in any other tumor cell line sample or in LU15. The similar band intensities and identical sizes of the DNA signals in all specimens also argued against the possibility of a heterozygous deletion or translocation of this gene, at least in the region analyzed. No change was found in HT29, suggesting that the semaphorin IV/NY-LU-12 fusion sequence in the GenBank probably represents a cloning artifact.



### SSCP and sequence analysis of NY-LU-12 in Lu15 tumor DNA.

The mapping of NY-LU-12 to the lung cancer *TSG* locus raised the possibility that an altered protein product due to mutational event may be the basis for the autologous immune recognition. This possibility was explored using DNA sequencing and single-strand confirmational polymorphism (SSCP) analysis.

The DNA sequence contained in the immunoreactive clone Lu15-251 (nucleotide 2518-3599 of NY-LU-12) was obtained from the normal counterpart by RT-PCR cloning using autologous normal lung tissue, and no mutations were found when compared to Lu15-251.

RT-PCR SSCP was then used to analyze the entire NY-LU-12 gene, comparing Lu15 tumor tissue and autologous normal lung tissue. To encompass the whole sequence, 10 sets of primer pairs were designed, each amplifying a range of 205 to 603 bps. For products >400bps, a restriction enzyme digestion step was added prior to the electrophoresis step to further reduce the fragment sizes and increase the assay sensitivity. Results showed no reproducible changes between normal and tumor tissues, and thus no evidence of mutation in Lu15 tumor cDNA. A representative set of SSCP analysis is shown in Fig. 5.

### Serological response to NY-LU-12 in lung cancer patient

The frequency of anti-NY-LU-12 response was examined among normal adult and patient sera using the phage plaque assay identical to the original immunoscreening procedure. Of 21 absorbed sera from allogeneic lung cancer patients, one (Lu22) reacted strongly with the Lu15-251 plaque at 1:1000 dilution, and another (Lu7) also reacted at 1:1000, but only weakly. Nineteen other lung cancer patient sera were non-reactive, nor were the sera from 16 healthy donors, 15 colon cancer, 5 breast cancer, 1 renal cancer, 1 prostate cancer, 1 esophageal cancer, and 1 melanoma patients.

### Example 10: Expression analysis of additional cancer associated nucleic acids

The clone RING 3 was isolated from breast SEREX analysis as LONY-Br-5 (see above). The gene was identified as homologous to the "bromodomain testis" gene (BRDT; GenBank accession number AF019085). Analysis of related genes identified BRDT as a gene expressed only in testis, which was then investigated by RT-PCR analysis as described above.

The primers used to perform RT-PCR had the following sequences:

BRDT F1: CAAGAAAGGCACTCAACAG (bp 543-563 of BRDT)

BRDT R1: TTCACTACTTGCTTTAACTGC (bp 776-797 of BRDT)

The meiotic protein H1T (Histone 1 Testis; GenBank accession number M60094) was

5 identified through a literature search for meiotic proteins (testis specific expression).

The primers used to perform RT-PCR had the following sequences:

H1F1: TGCCGAACCTCTCTGTGTC (bp 116-135 of H1T)

H1R1: GCTTCGTGTAGATTTAGGAATC (bp 344-366 of H1T)

10 Table 10: RT-PCR analysis

	<u>Normal Tissue</u>	<u>BRDT</u>	<u>H1T</u>
	mammary gland	-	-
	liver	-	-
15	small intestine	-	-
	brain	-	+/- (very weak)
	lung	-	-
	fetal brain	-	-
	placenta	+	+
20	kidney	-	-
	skeletal muscle	-	-
	pancreas	-	-
	adrenal gland	-	-
	heart	-	-
25	thymus	-	-
	uterus	-	-
	prostate	-	+/- (very weak)
	spleen	-	-
	Testis	+	+

	<u>Tumor Tissue</u>	<u>BRDT</u>	<u>H1T</u>
	Colon	0/6	0/6
35	Breast	0/6	6/6+
	Melanoma	0/12	3/12+
	Lung	8/26+	4/26+
	Renal	0/2	0/2
	Ovary	0/2	0/2
40	Esophageal	0/1	0/1

Gastric	0/1	0/1
Bladder	0/2	0/2

Lung cancer specific expression of BRDT was observed (see table above). BRDT was expressed only in normal testis and possibly in placenta. The expression analysis of H1T revealed that all breast tumor samples (6 of 6) and ~30% lung cancers and melanoma tissue samples expressed H1T. H1T was expressed in normal testis and possibly in placenta and brain.

### **Example 11: allogeneic serotyping**

To confirm the cancer associated expression of SEREX clones, allogenic sera screening of gastric cancer patients' sera was conducted. Sera from normal patients (gastritis) was used as a control for expression of the clones in non-gastric cancer. The screening procedure used was as described above for the SEREX screening, except for the absorption of anti-bacterial and anti-bacteriophage antibodies. The modifications were as follows.

Serum from a stomach cancer patient or a normal individual was diluted to 1:10 in TBS (Tris buffered saline; final volume 5 ml) and passed through a column (BIO-RAD Poly-Prep Chromatography Column, Hercules, CA, USA) containing 0.5 ml Sepharose-4B cross linked to E. coli Y1090 lysate and 0.5 ml Sepharose-4B cross linked to E. coli BNN97 (5 Prime 3 Prime, Inc, Boulder, CO, USA). After repeating the column chromatography 10 times, serum was then diluted to 1:100 in TBS containing 1% BSA and 0.02% sodium azide. To remove antibodies to bacteria and bacteriophages further, 10 ml absorbed serum was incubated overnight with a 82 mm nitrocellulose membrane on which XL-1 Blue MRF' bacteria and lambda ZAP Express phages (Stratagene, La Jolla, CA USA) were immobilized. The serum was stored at - 80°C until use. For allogeneic typing, an equal numbers of positive phage and negative phage were mixed and plated and processed by the standard SEREX screening procedure.

The results of the allogenic screening experiments follow:

**Table 11: Allogenic Sera Screening of SEREX Sequences from Gastric Patients**

Sequence		Isolated in Serex Patients	Allogenic Serotyping Gastric Cancer Sera	Allogenic Serotyping Normal Sera
Gene/Clone	Number			
RPB-J H-2K binding factor		SM1	6/12	6/16
Telomeric repeat binding protein		SM1	1/12	0/16
Ser/Thr protein kinase		SM1	1/12	0/16
SRY interacting protein-1		SM1	2/12	1/16
Sterol carrier protein X		SM1	2/12	0/16
Archain		SM1	1/12	1/16
HEM-1		SM1	2/12	1/16
Id-1 helix-loop-helix protein		SM1	1/12	0/16
helix-loop-helix transcription factor		SM1	1/12	0/16
Follistatin related precursor protein		SM1,CK, KM	6/12	0/16
Translation initiation factor eIF-4gamma		SM1,SS1, KM	5/12	2/16
M phase phosphoprotein I		SM1,SS1	8/12	5/16
Lysal tRNA synthase		SM1	1/12	0/16
Gelsolin		SM1	4/12	0/16
Zinc finger protein		SM1	1/12	1/16
Goliath		SM1	2/12	1/16
zhx-1		SM1	1/12	1/16
SG24		SM1,SS1, KM	5/12	0/16
SG132		SM1	3/12	0/16
S553		SM1	7/12	7/16
S134		SM1	3/12	0/16
S328		SM1	2/12	1/16
S365		SM1, KM	2/12	0/16

	FKBP25		KM, SS1	5/12	0/16
	Pros-27		KM, CK	3/12	1/16
	BS4		KM	1/12	1/16
	GnRH-II		KM	1/12	0/16
5	CTBP		KM	1/12	0/16
	ETF		KM	3/12	1/16
	KIAA0438		KM	1/12	5/16
	KIAA0367		KM	4/12	3/16
	APK1		KM	2/12	0/16
10	IPP		KM	1/12	0/16
	Tropomyosin		KM	1/12	0/16
	p63		KM	1/12	0/16
	KIAA0181		KM	1/12	0/16
	KIAA0349		KM	1/12	0/16
15	RPB1		KM	5/12	9/15
	PPIM		KM	1/12	-
	EB virus		KM	3/12	-
	G.KM073		KM	6/12	-
	G.KM403		KM	1/12	-
20	KM192		KM	1/12	-
	KM294		KM	1/12	-
	KM362		KM	1/12	-
	KM031		KM	1/12	-
	KM081		KM	3/12	-
25	KM201		KM	1/12	-
	KM1496		KM	1/12	-
	KM334		KM	1/12	-
	KM313		KM	1/12	-
	E-cad/Y		CK	1/12	0/16
30	IPBP		SS1	1/4	-
	OS-9		SS1	1/4	-

Kinesin light chain		SS1	1/4	-
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The screening results shown above confirm the association of the SEREX clones with cancer. There is a higher correlation of cancer and the expression of certain clones, in particular, 5 follistatin related precursor protein, the translation initiation factor eIF-4gamma, the unknown sequence SG24, the FK506-binding protein 25, and the unknown sequence G.KM073. These clones are well suited to serve as diagnostic indicators of disease and as targets for therapeutics (e.g., vaccine compositions) development.

#### 10 **Example 12: Preparation of recombinant cancer associated antigens**

To facilitate screening of patients' sera for antibodies reactive with cancer associated antigens, for example by ELISA, recombinant proteins are prepared according to standard procedures. In one method, the clones encoding cancer associated antigens are subcloned into a baculovirus expression vector, and the recombinant expression vectors are introduced into 15 appropriate insect cells. Baculovirus/insect cloning systems are preferred because post-translational modifications are carried out in the insect cells. Another preferred eukaryotic system is the *Drosophila* Expression System from Invitrogen. Clones which express high amounts of the recombinant protein are selected and used to produce the recombinant proteins. The recombinant proteins are tested for antibody recognition using serum from the patient which was used to isolated 20 the particular clone, or in the case of cancer associated antigens recognized by allogeneic sera, e.g. certain breast cancer and gastric cancer associated antigens, by the sera from any of the patients used to isolate the clones or sera which recognize the clones' gene products.

Alternatively, the cancer associated antigen clones are inserted into a prokaryotic expression vector for production of recombinant proteins in bacteria. Other systems, including yeast expression 25 systems and mammalian cell culture systems also can be used.

#### **Example 13: Preparation of antibodies to cancer associated antigens**

The recombinant cancer associated antigens produced as in Example 12 above are used to generate polyclonal antisera and monoclonal antibodies according to standard procedures. The 30 antisera and antibodies so produced are tested for correct recognition of the cancer associated

antigens by using the antisera/antibodies in assays of cell extracts of patients known to express the particular cancer associated antigen (e.g. an ELISA assay). These antibodies can be used for experimental purposes (e.g. localization of the cancer associated antigens, immunoprecipitations, Western blots, etc.) as well as diagnostic purposes (e.g., testing extracts of tissue biopsies, testing for the presence of cancer associated antigens).

**Example 14: Expression of cancer associated antigens in cancers of similar and different origin.**

The expression of one or more of the cancer associated antigens is tested in a range of tumor samples to determine which, if any, other malignancies should be diagnosed and/or treated by the methods described herein. Tumor cell lines and tumor samples are tested for cancer associated antigen expression, preferably by RT-PCR according to standard procedures. Northern blots also are used to test the expression of the cancer associated antigens. Antibody based assays, such as ELISA and western blot, also can be used to determine protein expression. A preferred method of testing expression of cancer associated antigens (in other cancers and in additional same type cancer patients) is allogeneic serotyping using a modified SEREX protocol (as described above for gastric clones).

In all of the foregoing, extracts from the tumors of patients who provided sera for the initial isolation of the cancer associated antigens are used as positive controls. The cells containing recombinant expression vectors described in the Examples above also can be used as positive controls.

The results generated from the foregoing experiments provide panels of multiple cancer associated nucleic acids and/or polypeptides for use in diagnostic (e.g. determining the existence of cancer, determining the prognosis of a patient undergoing therapy, etc.) and therapeutic methods (e.g., vaccine composition, etc.).

**Example 15: HLA typing of patients positive for cancer associated antigen**

To determine which HLA molecules present peptides derived from the cancer associated antigens, cells of the patients which express the cancer associated antigens are HLA typed. Peripheral blood lymphocytes are taken from the patient and typed for HLA class I or class II, as

well as for the particular subtype of class I or class II. Tumor biopsy samples also can be used for typing. HLA typing can be carried out by any of the standard methods in the art of clinical immunology, such as by recognition by specific monoclonal antibodies, or by HLA allele-specific PCR (e.g. as described in WO97/31126).

5

**Example 16: Characterization of breast cancer associated antigen peptides presented by MHC class I and class II molecules.**

Antigens which provoke an antibody response in a subject may also provoke a cell-mediated immune response. Cells process proteins into peptides for presentation on MHC class I or class II molecules on the cell surface for immune surveillance. Peptides presented by certain MHC/HLA molecules generally conform to motifs. These motifs are known in some cases, and can be used to screen the breast cancer associated antigens for the presence of potential class I and/or class II peptides. Summaries of class I and class II motifs have been published (e.g., Rammensee et al., *Immunogenetics* 41:178-228, 1995). Based on the results of experiments such as those described in Example 15, the HLA types which present the individual breast cancer associated antigens are known. Motifs of peptides presented by these HLA molecules thus are preferentially searched.

One also can search for class I and class II motifs using computer algorithms. For example, computer programs for predicting potential CTL epitopes based on known class I motifs has been described (see, e.g., Parker et al, *J. Immunol.* 152:163, 1994; D'Amaro et al., *Human Immunol.* 43:13-18, 1995; Drijfhout et al., *Human Immunol.* 43:1-12, 1995). HLA binding predictions can conveniently be made using an algorithm available via the Internet on the National Institutes of Health World Wide Web site at URL <http://bimas.dcrt.nih.gov>. Methods for determining HLA class II peptides and making substitutions thereto are also known (e.g. Strominger and Wucherpfennig (PCT/US96/03182)).

The lung cancer SEREX clone polypeptides NY-LU-12 and NY-LU-12B (variant B), SEQ ID NOs: 708 and 710, were subjected to the HLA binding peptide analysis described above, using the NIH website, to identify HLA binding peptides for several common HLA molecules (HLA-A1, A2, A3, A24, B7, B44, and B52). The results are listed below in Table 12.

Table 12: Identification of HLA binding peptides in lung SEREX clones



	HLA	peptide	amino acids of NY-LU-12 protein	SEQ ID NO
	A1	NVEE-HSFSY	67 - 75	713
		PVDP-NILDY	287 - 295	714
5		DTDY-RSMEY	398 - 406	715
	A2	SLLE-DAIGC	506 - 514	716
		TLMI-QDKEV	521 - 529	717
		YVSSLDFWYC	533 - 542	718
10		VIVEVLEPYV	671 - 680	719
		KLTD-WNKLA	948 - 956	720
		QLSDLHKQNL	975 - 984	721
		KQSEQELAYL	991 - 1000	722
		KLVDKEDIDT	1042 - 1051	723
15		VMFA-RYKEL	1114 - 1122	724
	A3	QMFG-YGQSK	417 - 425	725
		GMPVKNLQLK	481 - 490	726
		GLPE-EEEIK	823 - 831	727
20		LLCRRQFPNK	958 - 967	728
	A24	EYRD-VDHRL	405 - 413	729
		GYVC-VEFSL	499 - 507	730
		DYGY-VCVEF	497 - 505	731
25		WYCKRCKANI	540 - 549	732
		TYPQPQKTSI	574 - 583	733
		IYRSTPPEVI	663 - 672	734
		HYYQ-GKKYF	754 - 762	735
		VYVP-QDPGL	816 - 824	736
30				
	B7	WNRDYPPPPL	26 - 35	737
		MPPV-DPNIL	285 - 293	738
		TARD-AQRDL	432 - 440	739
		GPSEEKPSRL	448 - 457	740
35		TPPEVIVEVL	667 - 676	741
		RVMFARYKEL	1113 - 1122	742
	B44	REMG-SCMEF	272 - 280	743
		EEQSSDAGLF	376 - 385	744
40		KEYN-TGYDY	490 - 498	745
		TEAKQELITY	566 - 575	746
		VEALRVVKIL	710 - 719	747
		GEYG-GDSYD	906 - 914	748
		LERREREGKF	1000 - 1009	749

- 86 -

B52	RQDGESKTIM	650	-	659	750
	TPPEVIVEVL	667	-	676	751
	YGFIDLDSHV	701	-	710	752
	RQFP-NKEVL	962	-	970	753

5

## NY-LU-12B (variant B)

10	A1	NVEE-HSFSY	121 - 129	754
		PVDP-NILDY	341 - 349	755
		DTDY-RSMEY	452 - 460	756

15	A2	WQSA-RFYYL	41 - 49	757
		SLLE-DAIGC	560 - 568	758
		TLMI-QDKEV	575 - 583	759
		YVSSLDFWYC	587 - 596	760
		VIVEVLEPYV	725 - 734	761
20		KLTD-WNKLA	1002 - 1010	762
		QLSDLHKQNL	1029 - 1038	763
		KQSEQELAYL	1045 - 1054	764
		KLVDKEDIDT	1096 - 1105	765
		VMFA-RYKEL	1168 - 1176	766

25	A3	QMFG-YGQSK	471 - 479	767
		GMPVKNLQLK	535 - 544	768
		GLPE-EEEIK	877 - 885	769
		LLCRRQFPNK	1012 - 1021	770

30	A24	YYLN-ATDVL	47 - 55	771
		FYYLNATDVL	46 - 55	772
		EYRD-VDHRL	459 - 467	773
		GYVC-VEFSL	553 - 561	774
		DYGY-VCVEF	551 - 559	775
		WYCKRCKANI	594 - 603	776
35		TYPQPQKTSI	628 - 637	777
		IYRSTPPEVI	717 - 726	778
		HYYQ-GKKYF	808 - 816	779
		VYVP-QDPGL	870 - 878	780

40	B7	WNRDYPPL	80 - 89	781
		MPPV-DPNIL	339 - 347	782
		TARD-AQRDL	486 - 494	783
		GPSEEKPSRL	502 - 511	784
		TPPEVIVEVL	721 - 730	785
45		RVMFARYKEL	1167 - 1176	786

5	B44	SEAWSSNEKF	59 - 68	787
		REMG-SCMEF	326 - 334	788
		EEQSSDAGLF	430 - 439	789
		KEYN-TGYDY	544 - 552	790
		TEAKQELITY	620 - 629	791
		VEALRVVKIL	764 - 773	792
		GEYG-GDSY	960 - 968	793
10		LERREREGKF	1054 - 1063	794
	B52	RQDGESKTIM	704 - 713	795
		TPPEVIVEVL	721 - 730	796
		YGFIDLDSHV	755 - 764	797
		RQFP-NKEVL	1016 - 1024	798

- 15 Likewise, other clones identified herein can be analyzed for the presence of candidate HLA binding peptides using no more than routine experimentation.

#### Example 17: Identification of the portion of a cancer associated polypeptide encoding an antigen

- 20 To determine if the cancer associated antigens isolated as described above can provoke a cytolytic T lymphocyte response, the following method is performed. CTL clones are generated by stimulating the peripheral blood lymphocytes (PBLs) of a patient with autologous normal cells transfected with one of the clones encoding a cancer associated antigen polypeptide or with irradiated PBLs loaded with synthetic peptides corresponding to the putative protein and matching
- 25 the consensus for the appropriate HLA class I molecule (as described above) to localize an antigenic peptide within the cancer associated antigen clone (*see, e.g., Knuth et al., Proc. Natl. Acad. Sci. USA* 81:3511-3515, 1984; van der Bruggen et al., *Eur. J. Immunol.* 24:3038-3043, 1994). These CTL clones are screened for specificity against COS cells transfected with the cancer associated antigen clone and autologous HLA alleles as described by Brichard et al. (*Eur. J. Immunol.* 26:224-230,
- 30 1996). CTL recognition of a cancer associated antigen is determined by measuring release of TNF from the cytolytic T lymphocyte or by <sup>51</sup>Cr release assay (Herin et al., *Int. J. Cancer* 39:390-396, 1987). If a CTL clone specifically recognizes a transfected COS cell, then shorter fragments of the cancer associated antigen clone transfected in that COS cell are tested to identify the region of the gene that encodes the peptide. Fragments of the cancer associated antigen clone are prepared by

exonuclease III digestion or other standard molecular biology methods. Synthetic peptides are prepared to confirm the exact sequence of the antigen.

Optionally, shorter fragments of cancer associated antigen cDNAs are generated by PCR. Shorter fragments are used to provoke TNF release or  $^{51}\text{Cr}$  release as above.

5 Synthetic peptides corresponding to portions of the shortest fragment of the cancer associated antigen clone which provokes TNF release are prepared. Progressively shorter peptides are synthesized to determine the optimal cancer associated antigen tumor rejection antigen peptides for a given HLA molecule.

10 A similar method is performed to determine if the cancer associated antigen contains one or more HLA class II peptides recognized by CTLs. One can search the sequence of the cancer associated antigen polypeptides for HLA class II motifs as described above. In contrast to class I peptides, class II peptides are presented by a limited number of cell types. Thus for these experiments, dendritic cells or B cell clones which express HLA class II molecules preferably are used.

15 EQUIVALENTS

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

20 All references disclosed herein are incorporated by reference in their entirety.

We claim:

## TABLE 1

## SEQ ID NO. 1:

- 5 U72994, AC004022, Z68323, AE001160, L34078, AF064863, AC002132, U60440, X66494, N21242, AA678312, W86762, R01605, AA782843, AA275156, W41927, AA874648, AA571241, AA562747, W10480, AA451301, AA866631, AA466667, AA999057, AI029140.

## 10 SEQ ID NO. 2:

AC004022, U72994, AC002420, AC004125, AA690961, W41927, AA874648, AC004022, U72994, AC002420, AC004125, AA690961, W41927, AA874648.

## 15 SEQ ID NO. 3:

- X98371, AL009008, L31790, Z83220, X92946, AC003975, AF008916, U80460, X75544, X66732, X95275, X52177, X07976, AC004451, Z74307, AB000878, AL009179, AF038667, 20 Z78544, Z48008, U23486, J05096, AB000882, Z30213, L11593, U18530, L27325, AC005191, M99579, AA130270, AA158245, AA903098, AI018453, AA436455, AA980593, AA172479, AA637487, AA116588, AA426854, AA050404, AA390025, AI006618, AI048382, C85944, AA673480, AI006510, AA823338, AA413694, W35075, AA015033, AA413584, W29693, AA637069, AA619839, AA125149, AA039004, AA674696, AA871138, AA414747, 25 AA198099, C91478, F071359, AA925957, AA820054, H16496, AI043756, AA892435, AA893551, AA818669, AA892785, AA944026, D33919, N96570, F19798, AI045451, AA800662, D65187, AA944025, AA925731, AA892314, AA945449.

## 30 SEQ ID NO. 4:

AA900930, AA925665.

## 35 SEQ ID NO. 5:

- U58105, Z81485, Z54236, Z48584, U61375, M55267, M59856, X51942, U77302, Z48621, AF032455, Z11866, AB013392, L32792, AA871997, AA084083, AA130829, AA083063, AA666290, N38894, D54459, T28921, AA806015, AA512059, AI043087, AI042894, 40 AA968324, AA238493, AA237462, AI042885, AI046424, AI035670, AA269430, AA250621, AI035540, AA260613, AA106870, AA238658, AA106134, AI042683, AA105958, AA144007, AA986558, AA457910, AA389400, AA673056, AA153254, AA754678, AI021109, AA390813, C36687, T41571, AI011183, AI013356, AI011739, AI030260, AA924384, C44421.

## 45 SEQ ID NO. 6:

AF036717, U91327, AF036718, U56248, Z48795, Z99290, M30697, U58204, M24417, AF022983, M33581, AC004619, H64641, AA477478, AA369676, AA088359, AA057574,

AA683066, AA446279, AA332363, T09328, R80982, AA069486, AA410842, C18527, AA293033, H12730, AA287344, AA029631, R83063, AA061290, AA185993, AA880204, AA499308, AA183172, AA242360, AA792388, AA175587, AA277140, AA880395, AA899046, AA859550, C35363, C35702, C32682, F14140, T18049, C83149, T45787, 5 AA924623, D47525, Z30723, AA897884, AA042465, AI009871, AA875198, C83016.

## SEQ ID NO. 7:

10 X74116, AL022148, AC004548, AC000352, Z11664, Z78065, Z74028, AE000163, AE000750, X74229, D90700, R59414, AA176708, W02568, AA354664, R43017, AA973553, F10008, D61827, AA826300, Z41398, T77572, R40189, H85823, W86541, T17276, AA679337, X83357, AA184845, AA416260, AA475603, AA388692, AA764445, AA388689, AA219880, AA290020, AA388507, AA387267, C86741, AA414436, AA451259, AA413796, AA930916, 15 AA793690, AA619447, AA062257, AA522026, AA816247, AA892032, AA817702, H33461, AA925507, AA849449, AI029236, AA247069, AA697975, AA882508, AA893258, AA698410, AA891755, AA698227, AA892782, AA899328, T04373, AA567522, AA698408, AA202615, AA141016, AA697974, AA697998, C61176, D69691, AI030205, AA586054.

## SEQ ID NO. 8:

20 U08218, L38909, Y11095, AC002431, Z23069, S77418, U39060, L38580, AF053367, Z36506, M18102, J03624, AA102264, AA730686, H47968, AA357170, AA130974, C06054, 25 AA626429, F00559, AA604528, AA383348, AA040127, N84965, D54884, D54883, R94309, AA373184, AA128091, W68194, H58283, R76347, AA343938, AA305144, AI049611, AA384516, AA720553, N57395, R97387, D52674, AA169408, H66293, AA456362, T74258, AA730145, AA101952, N86388, AA355003, AA307640, AA385679, AA354542, N99075, N83528, H87678, R84494, R35720, AA670111, AA186452, W32370, D55392, W05161, 30 AA641280, AA120503, C77063, AA146393, AA620177, AA509478, C77481, AA427148, AA474531, W83304, AA207424, AA763436, AA958473, AA799243, AA493061, AA967792, AA145256, AA089338, AA756259, AA789767, AA980112, AA866640, AA914516, AA821675, AA466770, AA015387, AA816036, AA246546, AA941789, AA955779, AA997768, AA997534, T43805, AA956150, T18836, T23333, AA525666, T18787, AA800483, 35 C64685, AA851367, C91730, AA143899, T23399.

## SEQ ID NO. 9:

40 AP000056, U43491, Z74919, L81498, Z94054, AC002503, L81499, AA740188, AA630241, AA974724, AA806907, N88859, N98242, H12649, R06485, R06511, AA546258, C76846, AA208416, AA959219, AA276381, W10055, AA462844, AA444278, W13447, W97802, AA542324, AA137880, AA269331, AA175695, W59029, AA003372, AA146233, AI045761, C93154, C94084, C94208, D68027, C12780, AA687005, AA080598, C12876, C12390, 45 AA848674, AA924440, T15031, AA451569, H35524.

## SEQ ID NO. 10:

U25640, AA127328, H24207, H08275, AA283063, AA826096, AA417382, AA464874, W05562, AA453370, N51211, AA495859, R33871, H00927, AA623997, AA220442, AA178568, AA605493, AA394557, AA956116, AA999037, AA818246.

5

SEQ ID NO. 11:

AB001740, AF039956, AA581972, AA594539, AA236870, AA464410, AA237069, AA694199, AI038896, AA167314, AA577381, AA430117, N23143, R53610, W37647, 10 AA724229, AA313202, AA860618, W16866, AA134966, AA255556, AA305224, R50528, AA844913, W32042, W37383, AA908394, W93357, W31353, R55254, N79251, AA456077, AA477700, AA477701, AA989005, AA455580, N32722, N22935, R50622, AA135047, R51941, T34020, T30416, T32309, AA883332, W93445, AA166984, AA026749, T08224, AA255572, W03768, AA033670, W31880, AA772832, AA230974, AA511207, W82274, 15 AA230365, AA671085, AA511230, AA606681, AA023735, AA444535, W98518, W14718, W85455, AA980318, AA137525, AA035840, AA692158, AA007919, W48013, AA444534, AA981497, AA002566, W48089, W99869, AA960396, AA960580, AA145259, AA145683, AA388960, AA389941, AA266272, AA145124, AA267212, AA959753, AA407991, A175818, AA943997, AA899476, AA899756, AA943998, AA955446, AA012783, AA924956, 20 AA892219, AA955331, AI012225, AA891436.

SEQ ID NO. 12:

U72994, AC004022, AF043493, U43252, U43251, U81830, U58105, U68242, Z93242, AL009029, M29872, U12980, M81118, M30471, Z56258, AF012943, AC004080, AC002563, AF024533, AF002991, Z63771, AP000042, AF064863, U80017, AC004087, Z55235, L05920, AA508139, N90748, AA450240, AA948158, AA828938, AA165115, AI003312, AA436633, AA419100, AA743442, AA961990, AA885286, AA861312, T84801, AI040166, AA494115, 30 AA652324, AA181105, AA095541, R59256, AA503712, AA700364, AA603821, T60326, AA779097, AI023884, AA603785, H79111, W39526, AA506607, W94361, N66078, R01605, H22694, W86762, W99303, AA745640, AA678312, AA431870, W41927, AA874648, C92734, C23102, C53080, C91168, D65098, C32959, C50029, M80125, C34452, C83862, C24659, T21473, AA874720, C06696, W43071, AI043300, C53907. 35

SEQ ID NO. 13:

X94232, U90437, AC003052, U59809, AC004001, M95396, Z67884, X77486, U70051, 40 X14805, AF022976, Z83823, X77485, J04171, AF036007, U05768, U88315, Z98048, AF036009, AC005179, U41277, U32517, AE001138, D64060, M84387, H29022, AA814221, N26314, AA935912, AA873506, AA608576, AA453605, AA232674, Z38725, AA772022, AA025212, AA318330, R48115, AA234084, H18508, N64543, AA970508, R36933, AA306944, H49559, AA325555, H85834, H89988, AA343974, AA648643, H65664, T62713, 45 H16554, N21122, AA351037, AA484621, AA221492, AA259314, C76383, C76336, AA607924, C76394, AA408562, AA921258, AI006352, W41405, AA153317, AA015435, AA027405, AA794066, AA498038, AA184222, AI011068, AA859614, AA899776, AA955080, AA799674, AA849652, AI009788, AA900928, AI007950, AA109392, AA753592, U92780, AA957632, AA567950, AI009495.

## SEQ ID NO. 14:

AC000075, U66140, R14195, AA220229, T31199, R19104, R19148, Z46126, AA417619,  
5 Z45284, H14105, R84666, AA090321, AA350108, W52840, R48497, R13097, T66255,  
W44467, AA247676, AA198489, AA388175, AA261453, AA237111, AA790730, AA162394,  
AA816498, AI013729, AA684961, AA979759.

## 10 SEQ ID NO. 15:

AF069301, D10651, U11419, U11287, M91562, U90278, U72724, X57855, X79424, M16512,  
M64542, Z14152, AF016667, L01488, Z75955, AF024504, M13968, W67775, AA934587,  
AA617696, AA913577, AA628682, W74527, AA969876, AA995606, AA622402, AA027090,  
15 AA620556, AA085733, AA187157, AI031865, AA972318, AA897169, W79046, AA531124,  
AA733183, T90909, Z25096, AA721771, AA115089, T49643, R00622, N93780, R00626,  
AA365494, T71475, N74066, AA027130, T83325, AA115569, AA658299, T55344, T83700,  
AA426250, AA393863, AA282967, R08138, AI000112, AA807574, AA077926, AA397527,  
W87761, AA243026, R56368, H16371, AA958697, AA003997, AA008542, AA036229,  
20 AA397074, AA250467, AA260498, AA968175, AA253686, AA727785, AI019478, AA474978,  
AA543461, AA990281, AA245791, AA617042, AA015355, AA983015, AA982200,  
AA120064, AA462778, AA242574, AA986993, AA986911, AA882490, AA223057,  
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AA851120.

## 25 SEQ ID NO. 16:

Z68106, X14199, M14872, Z63497, M31670, AC002123, Z63498, AA280070, AA215687,  
30 H93207, AA070367, W95534, AA682436, AA741066, AA173269, AA641255, AA215688,  
AA724798, N23259, AA442155, AA634563, AA074699, AA642322, AA861347, AA283655,  
AI002587, W95419, AA357042, AA761253, AA197191, T54480, AA133029, AA378991,  
AA114599, AA219925, AA174327, AA003800, C86661, AA990433, AA277014, AA445101,  
AA671205, AI036728, AA241221, AA213304, AI035350, W08919, W36663, AA061406,  
35 AA144736, AA240583, AI006563, AA980152, AA250075, AA088967, W17488, AA098269,  
W10200, AA543712, AA755434, AI012680, AA820868, AA949519, AA391130, AA202576,  
AA979150, AA012391, AA539472.

## 40 SEQ ID NO. 17:

J03592, M24103, AB009386, U44832, J02966, M24102, U27316, U10404, X70847, D12771,  
D12770, J02683, J03591, U27315, M76669, U39779, M13783, J04982, X74510, X61667,  
M57424, L78810, AC004000, Z75206, U68723, Z75207, AF009661, X53264, J03320, U66060,  
45 AB011800, M77194, AE000021, L07268, AE000936, U03115, AF009663, AA582128,  
AA916851, AA576667, AA915921, AA916853, N58735, AA428106, AA427849, AI024255,  
H69807, H11315, N36980, H69597, AA826334, W05080, N37044, AA385873, N48222,  
AA394173, AA837522, AI002511, AA292870, T96300, AA360716, AA379604, AA862844,  
AA430455, AA479859, AA133899, AA669954, H92542, AA095298, AA995794, AI003667,



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## SEQ ID NO. 18:

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## SEQ ID NO. 19:

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SEQ ID NO. 20:

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SEQ ID NO. 21:

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5 SEQ ID NO. 29:

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SEQ ID NO. 30:

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SEQ ID NO. 31:

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SEQ ID NO. 32:

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## SEQ ID NO. 109:

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SEQ ID NO. 119:

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SEQ ID NO. 121:

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SEQ ID NO. 125:

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SEQ ID NO. 127:

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002030-6263100

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SEQ ID NO. 131:

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SEQ ID NO. 135:

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SEQ ID NO. 141:

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SEQ ID NO. 143:

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SEQ ID NO. 145:

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SEQ ID NO. 147:

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SEQ ID NO. 149:

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SEQ ID NO. 151:

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SEQ ID NO. 153:

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SEQ ID NO. 155:

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SEQ ID NO. 157:

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SEQ ID NO. 167:

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SEQ ID NO. 169:

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SEQ ID NO. 170:

D32050, D16969, AC004423, S81497.

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SEQ ID NO. 172:

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SEQ ID NO. 174:

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40 \_SEQ ID NO: 176

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- 10 D15562, T20348, AA966363, AA949269, AA785774, AA728671, D16092, N37869, D48782.

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- 15 AA848184, AA280453.

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15 SEQ ID NO: 194

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45 SEQ ID NO: 198

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30 SEQ ID NO: 200

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35 SEQ ID NO:265

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15 SEQ ID NO: 270

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25 SEQ ID NO: 319

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35 SEQ ID NO: 320

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5 SEQ ID NO: 321

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SEQ ID NO: 322

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40 SEQ ID NO: 324

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35 SEQ ID NO: 327

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45 SEQ ID NO: 328

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15 SEQ ID NO: 329

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25 SEQ ID NO: 330

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40 SEQ ID NO: 333

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10 SEQ ID NO: 490

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25 SEQ ID NO: 491

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SEQ ID NO: 510

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25 SEQ ID NO: 512

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SEQ ID NO: 513

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45 SEQ ID NO: 514

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SEQ ID NO: 517

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5 SEQ ID NO: 519

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40 SEQ ID NO: 539

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**DECLASSIFICATION AUTHORITY**

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25 X63773, Z92547, U51244, AL009173, AC002402, AC004613, AC001608, AC002486,  
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30 AA468571, AA493584, N26697, AA252846, AA493971, AA132716, T29138, AA069204,  
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D43920, U26259, L04656, X15209, AF020312, U88713, U88712, S80994, AA890595,  
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45 AA576448, AA594332, AA554043, AA151140, AI049688, W95685, AI041568, AA492300,  
H29466, H29465, H50770, AA081057, R42909, AA083642, H91241, H50360, T52344,

N26936, N66716, H68058, AA928951, AA280393, AA934109, AA505844, AA355104, AA504565, D45524, R17569, F04483, T23042, AA247255, H61892, AI003120, D60896, AA442117, AI041522, AA301168, H92604, AA480590, AA989528, F08851, AA612865, F08256, AA969568, T52417, AA632042, AI038369, AA079461, AA367105, AA322594, 5 AA902644, AA814598, AA372751, AA573311, U33921, H92264, W95714, AA679052, AA079462, H50677, AA825284, N80152, AA436772, AA325582, AA737681, AA770224, AA812204, R52021, R87930, R50149, AA298850, AA569993, H26500, H98164, N22864, AA281862, H72485, W28236, W38896, W76200, AA397991, AA326213, AA406569, AA810203, N26696, AA607276, AF064939, AA549397, AA718492, W11974, AA790829, 10 AA718494, AA241183, AA086694, AA914805, AA823956, AA209543, AA268319, AA794261, AI042691, C80539, AA675676, AA794590, AA930627, AA795177, AA863563, AA607084, AA794703, AA960471, C85885, AA260352, AI044485, AA851524, AA851651, AA979509, H31962, AI008699, AA539524, D48514, AA440856, C74456.

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W52500, W52500 zd13d02.r1 Soares fetal heart NbHH19W Homo sap... 728 0.0  
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AA057030, AA057030 zk78b03.r1 Soares pregnant uterus NbHPU Ho... 698 0.0  
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AA116072, AA116072 zm79e11.r1 Stratagene neuroepithelium (#93... 678 0.0  
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H69274, H69274 EST00070 Homo sapiens cDNA clone HE6WCR117 5'. 658 0.0  
AA047371, AA047371 zk78b03.s1 Soares pregnant uterus NbHPU Ho... 658 0.0  
R64669, R64669 yi22c09.r1 Homo sapiens cDNA clone 139984 5'. 654 0.0  
AA116073, AA116073 zm79e11.s1 Stratagene neuroepithelium (#93... 634 e-180  
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AA425945, AA425945 zv84a12.s1 Soares total fetus Nb2HF8 9w Ho... 595 e-168  
AA436368, AA436368 zv32f05.s1 Soares ovary tumor NbHOT Homo s... 585 e-165  
AA975130, AA975130 on06f01.s1 NCI\_CGAP\_Lei2 Homo sapiens cDNA... 579 e-163  
AA885226, AA885226 am34e06.s1 Soares NFL T GBC S1 Homo sapien... 559 e-157  
AA912472, AA912472 ol96e03.s1 NCI\_CGAP\_PNS1 Homo sapiens cDNA... 555 e-156  
AA320935, AA320935 EST23388 Adipose tissue, white II Homo sap... 553 e-155

AA042872, AA042872 zk56b07.s1 Soares pregnant uterus NbHPU Ho... 543 e-152  
 T08932, T08932 EST06824 Homo sapiens cDNA clone HIBBM46 5' end. 537 e-150  
 AA488258, AA488258 ad08f07.r1 Soares NbHFB Homo sapiens cDNA ... 533 e-149  
 T19350, T19350 h03012t Testis 1 Homo sapiens cDNA clone h0301... 496 e-138  
 H87681, H87681 yw15e04.r1 Homo sapiens cDNA clone 252318 5'. 490 e-136  
 H81522, H81522 yu61h08.r1 Homo sapiens cDNA clone 230655 5'. 466 e-129  
 T49620, T49620 ya77g03.s1 Homo sapiens cDNA clone 67732 3'. 452 e-125  
 R14363, R14363 yf80d10.r1 Homo sapiens cDNA clone 28995 5' si... 446 e-123  
 AA211476, AA211476 zp75h11.s1 Stratagene HeLa cell s3 937216 ... 430 e-118  
 N46636, N46636 yy48a09.r1 Homo sapiens cDNA clone 276760 5'. 424 e-116  
 Z17358, HSDHII065 H. sapiens partial cDNA sequence; clone HI... 416 e-114  
 R40737, R40737 yf80d10.s1 Homo sapiens cDNA clone 28995 3'. 400 e-109  
 AA410278, AA410278 zv32f05.r1 Soares ovary tumor NbHOT Homo s... 383 e-104  
 AA496574, AA496574 zv37b03.s1 Soares ovary tumor NbHOT Homo s... 375 e-101  
 N34907, N34907 yy48a09.s1 Homo sapiens cDNA clone 276760 3'. 371 e-100  
 T49619, T49619 ya77g03.r1 Homo sapiens cDNA clone 67732 5'. 355 1e-95  
 AA301480, AA301480 EST14551 Thymus III Homo sapiens cDNA 5' end 341 2e-91  
 R31593, R31593 yh76f03.s1 Homo sapiens cDNA clone 135677 3'. 317 2e-84  
 AA984591, AA984591 am89d10.s1 Stratagene schizo brain S11 Hom... 313 4e-83  
 AA338831, AA338831 EST43831 Fetal brain I Homo sapiens cDNA 5... 238 2e-60  
 T07305, T07305 EST05194 Homo sapiens cDNA clone HFBEG86. 230 4e-58  
 AA159942, AA159942 zo79c05.r1 Stratagene pancreas (#937208) H... 204 3e-50  
 R57355, R57355 F2878 Fetal heart Homo sapiens cDNA clone F287... 196 6e-48  
 AA729237, AA729237 nx35c08.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 192 1e-46  
 AA877709, AA877709 nr09g11.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 172 9e-41  
 AA969195, AA969195 op51c03.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 107 4e-21  
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 AA983156, AA983156 oq51g09.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 66 2e-08  
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 T41169, T41169 ya31g10.s3 Homo sapiens cDNA clone 62274 3' co... 40 0.86  
 AA070108, AA070108 zm69d06.s1 Stratagene neuroepithelium (#93... 40 0.86  
 AA706183, AA706183 ag93e01.s1 Stratagene hNT neuron (#937233)... 40 0.86  
 AA393069, AA393069 zt69e09.r1 Soares testis NHT Homo sapiens ... 40 0.86  
 AA371600, AA371600 EST83650 Pituitary gland, subtracted (prol... 40 0.86  
 AA977820, AA977820 oq78a09.s1 NCI\_CGAP\_Kid6 Homo sapiens cDNA... 38 3.4  
 AA584760, AA584760 no04c06.s1 NCI\_CGAP\_Phe1 Homo sapiens cDNA... 38 3.4  
 AA584615, AA584615 no08g12.s1 NCI\_CGAP\_Phe1 Homo sapiens cDNA... 38 3.4  
 AA229827, AA229827 nc48c04.r1 NCI\_CGAP\_Pr3 Homo sapiens cDNA ... 38 3.4  
 W21398, W21398 zb50a11.r1 Soares fetal lung NbHL19W Homo sapi... 38 3.4

AA136933, AA136933 zn97f07.s1 Stratagene fetal retina 937202 ... 38 3.4

AA869501, AA869501 vq08g11.r1 Barstead stromal cell line MPLR... 833 0.0  
 AA221749, AA221749 my28g01.r1 Barstead mouse pooled organs MP... 789 0.0  
 AA271363, AA271363 va71d08.r1 Soares mouse 3NME12 5 Mus muscu... 781 0.0  
 AA544727, AA544727 vk35d01.r1 Soares mouse mammary gland NbMM... 773 0.0  
 W84968, W84968 mf42e02.r1 Soares mouse embryo NbME13.5 14.5 M... 640 0.0  
 AA153324, AA153324 ms61e11.r1 Stratagene mouse embryonic carc... 617 e-175  
 AA673899, AA673899 vo86g07.r1 Barstead mouse irradiated colon... 583 e-164  
 AA797488, AA797488 vw28a05.r1 Soares mouse mammary gland NbMM... 519 e-145  
 W71831, W71831 me45b06.r1 Soares mouse embryo NbME13.5 14.5 M... 472 e-131  
 AA213358, AA213358 mu74e04.r1 Stratagene mouse embryonic carc... 444 e-123  
 W75918, W75918 me82f05.r1 Soares mouse embryo NbME13.5 14.5 M... 444 e-123  
 AA038141, AA038141 mi81e05.r1 Soares mouse p3NMF19.5 Mus musc... 359 3e-97  
 AA038288, AA038288 mi83b04.r1 Soares mouse p3NMF19.5 Mus musc... 323 1e-86  
 AA017742, AA017742 mh40c03.r1 Soares mouse placenta 4NbMP13.5... 297 8e-79  
 AA771297, AA771297 vt17g04.r1 Barstead mouse myotubes MPLRB5 ... 297 8e-79  
 AA105228, AA105228 mp45b11.r1 Barstead MPLRB1 Mus musculus cD... 295 3e-78  
 AA068340, AA068340 mm53f01.r1 Stratagene mouse embryonic carc... 293 1e-77  
 AA612347, AA612347 vo05c08.r1 Stratagene mouse skin (#937313)... 281 5e-74  
 AA038300, AA038300 mi83d04.r1 Soares mouse p3NMF19.5 Mus musc... 270 2e-70  
 AA500952, AA500952 vg01h04.r1 Soares mouse NbMH Mus musculus ... 252 4e-65  
 W08368, W08368 mb41f07.r1 Soares mouse p3NMF19.5 Mus musculus... 212 4e-53  
 AA052280, AA052280 ma82e12.r1 Soares mouse p3NMF19.5 Mus musc... 123 3e-26  
 AA064466, AA064466 ml49c05.r1 Stratagene mouse testis (#93730... 107 2e-21  
 AA271566, AA271566 vb74b09.r1 Soares mouse 3NME12 5 Mus muscu... 60 3e-07  
 C86222, C86222 Mus musculus fertilized egg cDNA 3'-end seque... 42 0.078  
 W83632, W83632 mf31a04.r1 Soares mouse embryo NbME13.5 14.5 M... 42 0.078  
 AA423627, AA423627 ve80f01.r1 Soares mouse mammary gland NbMM... 42 0.078  
 AA036586, AA036586 mi41h08.r1 Soares mouse embryo NbME13.5 14... 42 0.078  
 AA207496, AA207496 mv78g02.r1 GuayWoodford Beier mouse kidney... 42 0.078  
 AA120433, AA120433 mp82h11.r1 Soares 2NbMT Mus musculus cDNA ... 42 0.078  
 W08185, W08185 mb42h02.r1 Soares mouse p3NMF19.5 Mus musculus... 38 1.2  
 AA065563, AA065563 ml71b06.r1 Stratagene mouse kidney (#93731... 38 1.2  
 AA288756, AA288756 mr46h07.r1 Life Tech mouse embryo 15 5dpc ... 38 1.2  
 AA119334, AA119334 mp80e10.r1 Soares 2NbMT Mus musculus cDNA ... 38 1.2  
 AA163051, AA163051 ms24a10.r1 Stratagene mouse skin (#937313)... 38 1.2  
 N28074, N28074 MDB1392R Mouse brain, Stratagene Mus musculus ... 38 1.2  
 AA288757, AA288757 mr46h08.r1 Life Tech mouse embryo 15 5dpc ... 38 1.2  
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AA840310, AA840310 vw91a10.r1 Stratagene mouse skin (#937313)... 36 4.8  
AA986428, AA986428 ue13b04.x1 Sugano mouse embryo mewa Mus mu... 36 4.8  
W47677, W47677 mc89g07.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.8  
AA057996, AA057996 mj56c10.r1 Soares mouse embryo NbME13.5 14... 36 4.8  
AA183858, AA183858 mo95h01.r1 Stratagene mouse testis (#93730... 36 4.8  
AA212232, AA212232 mu43e08.r1 Soares 2NbMT Mus musculus cDNA ... 36 4.8  
W41067, W41067 mc39a06.r1 Soares mouse p3NMF19.5 Mus musculus... 36 4.8  
AA967594, AA967594 uh01d06.r1 Soares mouse hypothalamus NMHy ... 36 4.8  
AA414093, AA414093 vc64c07.s1 Knowles Solter mouse 2 cell Mus... 36 4.8  
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AA874496, AA874496 vx03a08.r1 Soares 2NbMT Mus musculus cDNA ... 36 4.8  
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AA023983, AA023983 mh94a07.r1 Soares mouse placenta 4NbMP13.5... 36 4.8  
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AA274648, AA274648 vb08c01.r1 Soares mouse NML Mus musculus c... 36 4.8  
AA140347, AA140347 mq89g06.r1 Stratagene mouse heart (#937316... 36 4.8  
AA499377, AA499377 vi89c07.r1 Stratagene mouse heart (#937316... 36 4.8  
C88747, C88747 Mus musculus early blastocyst cDNA, clone 01B... 36 4.8  
AA726125, AA726125 vu88c06.r1 Stratagene mouse skin (#937313)... 36 4.8  
AA760311, AA760311 vv71c12.r1 Stratagene mouse skin (#937313)... 36 4.8  
AA763007, AA763007 vw60b05.r1 Soares mouse mammary gland NMLM... 36 4.8  
AA929878, AA929878 vz44d03.r1 Soares 2NbMT Mus musculus cDNA ... 36 4.8  
W59064, W59064 md67e10.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.8  
AA103519, AA103519 mo24b12.r1 Life Tech mouse embryo 13 5dpc ... 36 4.8  
AA222310, AA222310 my14d08.r1 Barstead mouse heart MPLRB3 Mus... 36 4.8  
W83557, W83557 mf32d02.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.8  
AA168631, AA168631 ms33c05.r1 Stratagene mouse skin (#937313)... 36 4.8  
AA960143, AA960143 vw60b05.s1 Soares mouse mammary gland NMLM... 36 4.8  
W34557, W34557 mc58a05.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.8  
W98818, W98818 mf94e06.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.8  
AA008527, AA008527 mg85h01.r1 Soares mouse embryo NbME13.5 14... 36 4.8  
AA008734, AA008734 mg86h03.r1 Soares mouse embryo NbME13.5 14... 36 4.8  
AA510568, AA510568 vg33a10.r1 Soares mouse mammary gland NbMM... 36 4.8  
AA672524, AA672524 vo59e11.r1 Soares mouse mammary gland NbMM... 36 4.8  
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AA096626, AA096626 mo09h06.r1 Life Tech mouse embryo 10 5dpc ... 36 4.8  
AA124880, AA124880 mp73e06.r1 Soares 2NbMT Mus musculus cDNA ... 36 4.8  
AA198005, AA198005 mv12b09.r1 GuayWoodford Beier mouse kidney... 36 4.8  
AA624213, AA624213 vm98h06.r1 Knowles Solter mouse blastocyst... 36 4.8  
AA521863, AA521863 vi08b01.r1 Barstead mouse myotubes MPLRB5 ... 36 4.8  
AA692113, AA692113 vt19d03.r1 Barstead mouse myotubes MPLRB5 ... 36 4.8  
W71551, W71551 me39e11.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.8

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AA875699, AA875699	TENU0170	T.cruzi epimastigote normalized c...	42	0.069
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C74504, C74504	Rice cDNA, partial sequence (E31753_1A)		40	0.27
AA698333, AA698333	HL04291.5prime	HL Drosophila melanogaster ...	38	1.1
AA441429, AA441429	LD16359.5prime	LD Drosophila melanogaster ...	38	1.1
N68770, N68770	TgESTzy35b12.r1	TgRH Tachyzoite cDNA Toxoplasm...	38	1.1
AA246440, AA246440	LD05311.5prime	LD Drosophila melanogaster ...	38	1.1
AA801776, AA801776	GM12975.5prime	GM Drosophila melanogaster ...	38	1.1
N69148, N69148	TgESTzy33d10.r1	TgRH Tachyzoite cDNA Toxoplasm...	38	1.1
AA536484, AA536484	LD17114.5prime	LD Drosophila melanogaster ...	38	1.1
AA392544, AA392544	LD11451.5prime	LD Drosophila melanogaster ...	38	1.1
AA202696, AA202696	LD03182.5prime	LD Drosophila melanogaster ...	38	1.1
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AA264629, AA264629	LD08245.5prime	LD Drosophila melanogaster ...	38	1.1
AA735318, AA735318	LD21104.5prime	LD Drosophila melanogaster ...	38	1.1
AA264558, AA264558	LD08333.5prime	LD Drosophila melanogaster ...	38	1.1
AA536476, AA536476	LD17106.5prime	LD Drosophila Embryo Drosop...	38	1.1
AA957774, AA957774	UI-R-E1-fv-f-04-0-UI.s1	UI-R-E1 Rattus nor...	38	1.1
AA567991, AA567991	HL02092.5prime	HL Drosophila melanogaster ...	38	1.1
AA957876, AA957876	UI-R-E1-fv-f-04-0-UI.s2	UI-R-E1 Rattus nor...	38	1.1
AA892488, AA892488	EST196291	Normalized rat kidney, Bento Soa...	38	1.1
AA699001, AA699001	HL06668.5prime	HL Drosophila melanogaster ...	36	4.3
C19706, C19706	Rice cDNA, partial sequence (E10809_1A)		36	4.3
D41773, RICS4574A	Rice cDNA, partial sequence (S4574_2A).		36	4.3
C40680, C40680	C.elegans cDNA clone yk247c4 : 5' end, single...		36	4.3
AA698625, AA698625	HL05354.5prime	HL Drosophila melanogaster ...	36	4.3
C82819, C82819	Oryctolagus cuniculus corneal endothelial cDN...		36	4.3
D46016, RICS10393A	Rice cDNA, partial sequence (S10393_3A).		36	4.3
AA536314, AA536314	LD16858.5prime	LD Drosophila melanogaster ...	36	4.3
AA801012, AA801012	EST190509	Normalized rat muscle, Bento Soa...	36	4.3
D46541, RICS11289A	Rice cDNA, partial sequence (S11289_1A).		36	4.3
D47315, RICS12612A	Rice cDNA, partial sequence (S12612_1A).		36	4.3
AA735857, AA735857	GM09977.5prime	GM Drosophila melanogaster ...	36	4.3
AA753921, AA753921	97BS0370	Rice Immature Seed Lambda ZAPII c...	36	4.3
D47243, RICS12505A	Rice cDNA, partial sequence (S12505_1A).		36	4.3
AA978395, AA978395	LD28411.5prime	LD Drosophila melanogaster ...	36	4.3

D15134, RICC0136A Rice cDNA, partial sequence (C0136A). 36 4.3  
 D46483, RICS11185A Rice cDNA, partial sequence (S11185\_1A). 36 4.3  
 D46618, RICS11395A Rice cDNA, partial sequence (S11395\_1A). 36 4.3  
 D46659, RICS11457A Rice cDNA, partial sequence (S11457\_1A). 36 4.3  
 D46719, RICS11572A Rice cDNA, partial sequence (S11572\_1A). 36 4.3  
 D48579, RICS14880A Rice cDNA, partial sequence (S14880\_2A). 36 4.3  
 AA802334, AA802334 GM04219.5prime GM Drosophila melanogaster ... 36 4.3  
 D46066, RICS10470A Rice cDNA, partial sequence (S10470\_1A). 36 4.3  
 D47037, RICS12104A Rice cDNA, partial sequence (S12104\_1A). 36 4.3  
 D46874, RICS11807A Rice cDNA, partial sequence (S11807\_2A). 36 4.3  
 D47174, RICS12340A Rice cDNA, partial sequence (S12340\_2A). 36 4.3  
 T04578, T04578 625 Lambda-PRL2 Arabidopsis thaliana cDNA clon... 36 4.3  
 C83675, C83675 Oryctolagus cuniculus corneal endothelial cDN... 36 4.3  
 D47950, RICS13762A Rice cDNA, partial sequence (S13762\_1A). 36 4.3  
 R90044, R90044 16399 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 36 4.3  
 D46994, RICS12013A Rice cDNA, partial sequence (S12013\_2A). 36 4.3  
 AA440820, AA440820 LD15713.5prime LD Drosophila melanogaster ... 36 4.3  
 C72089, C72089 Rice cDNA, partial sequence (E0963\_1A) 36 4.3  
 Z84004, SSZ84004 S.scrofa mRNA; expressed sequence tag (5'; ... 36 4.3  
 D47519, RICS13070A Rice cDNA, partial sequence (S13070\_1A). 36 4.3  
 C19735, C19735 Rice cDNA, partial sequence (E10858\_1A) 36 4.3  
 D47231, RICS12462A Rice cDNA, partial sequence (S12462\_1A). 36 4.3  
 D47147, RICS12293A Rice cDNA, partial sequence (S12293\_1A). 36 4.3  
 AA950198, AA950198 LD30147.5prime LD Drosophila melanogaster ... 36 4.3  
 Z47624, ATTS4480 A. thaliana transcribed sequence; clone TAI... 36 4.3  
 D45955, RICS10259A Rice cDNA, partial sequence (S10259\_1A). 36 4.3  
 D47137, RICS12280A Rice cDNA, partial sequence (S12280\_1A). 36 4.3  
 D69927, CELK093H2F C.elegans cDNA clone yk93h2 : 5' end, sin... 36 4.3  
 AA392275, AA392275 LD11117.5prime LD Drosophila melanogaster ... 36 4.3

SEQ ID NO:546

D87455, D87455 Human mRNA for KIAA0266 gene, complete cds 1164 0.0  
 Z99129, HS425C14 Human DNA sequence from clone 425C14 on chr... 42 0.20  
 D90900, D90900 Synechocystis sp. PCC6803 complete genome, 2/... 40 0.80  
 Z74281, SCYDL233W S.cerevisiae chromosome IV reading frame O... 38 3.1  
 AL021528, HS394P21 Homo sapiens DNA sequence from PAC 394P21... 38 3.1  
 Z49155, HSL83D3 Human DNA from cosmid L83d3, Huntington's Di... 38 3.1  
 U33761, HSU33761 Human cyclin A/CDK2-associated p45 (Skp2) mR... 38 3.1  
 AF052832, AF052832 Trypanosoma cruzi CL Brener cosmid 1b21 ch... 38 3.1  
 Z98600, SPAC20G4 S.pombe chromosome I cosmid c20G4 38 3.1



Y09438, SPHUSPLUS *S.pombe* hus1+ gene 38 3.1  
 D29951, MUSKIF Mouse mRNA for kinesin family protein KIF1a, ... 38 3.1

# HUMAN ESTs

AA151187, AA151187 zo03c11.r1 Stratagene colon (#937204) Homo... 694 0.0  
 AA824593, AA824593 oc83d10.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 670 0.0  
 AA954862, AA954862 op20c03.s1 NCI\_CGAP\_Co12 Homo sapiens cDNA... 581 e-164  
 T16360, T16360 NIB1193 Normalized infant brain, Bento Soares ... 517 e-145  
 R54592, R54592 yg81h10.s1 Homo sapiens cDNA clone 40102 3'. 511 e-143  
 AA373594, AA373594 EST85631 HSC172 cells I Homo sapiens cDNA ... 507 e-142  
 AA100660, AA100660 zl90a05.r1 Stratagene colon (#937204) Homo... 383 e-104  
 R42009, R42009 yg05b04.s1 Homo sapiens cDNA clone 31336 3'. 379 e-103  
 AA249614, AA249614 k3041.seq.F Human fetal heart, Lambda ZAP ... 252 5e-65  
 AA360633, AA360633 EST69800 T-cell lymphoma Homo sapiens cDNA... 182 4e-44  
 AA053498, AA053498 zl70b11.r1 Stratagene colon (#937204) Homo... 38 1.5  
 AA992442, AA992442 or85h03.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 38 1.5

AA065677, AA065677 mm43c03.r1 Stratagene mouse melanoma (#937... 297 4e-79  
 AA529728, AA529728 vi38g12.r1 Beddington mouse embryonic regi... 42 0.035  
 W91608, W91608 MTA.D10.092.A MTA adult mouse thymus library M... 42 0.035  
 AA177186, AA177186 mt51a11.r1 Stratagene mouse embryonic carc... 42 0.035  
 AA048008, AA048008 mj26h10.r1 Soares mouse embryo NbME13.5 14... 36 2.2  
 AA637535, AA637535 vu10c02.r1 Barstead mouse myotubes MPLRB5 ... 36 2.2  
 AA726355, AA726355 vu90c09.r1 Stratagene mouse skin (#937313)... 36 2.2  
 AA404025, AA404025 va31c11.r1 GuayWoodford Beier mouse kidney... 36 2.2  
 AA060014, AA060014 ml34d07.r1 Stratagene mouse testis (#93730... 36 2.2  
 AA870617, AA870617 vq23h10.r1 Barstead stromal cell line MPLR... 36 2.2  
 AA414112, AA414112 vc64f08.s1 Knowles Solter mouse 2 cell Mus... 36 2.2  
 AA764250, AA764250 vv49e09.r1 Soares 2NbMT Mus musculus cDNA ... 36 2.2

H34350, H34350 EST111226 Rat PC-12 cells, NGF-treated (9 days... 36 1.9  
 C40718, C40718 *C.elegans* cDNA clone yk247f9 : 5' end, single... 36 1.9  
 AA817925, AA817925 UI-R-A0-af-g-04-0-UI.s1 UI-R-A0 Rattus nor... 36 1.9  
 AA955650, AA955650 UI-R-E1-fc-e-10-0-UI.s1 UI-R-E1 Rattus nor... 36 1.9

SEQ ID NO:547

002050-000000

U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.35  
 U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.35  
 AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.35  
 U85773, HSU85773 Human phosphomannomutase (PMM2) mRNA, comple... 40 1.4  
 Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 1.4  
 AC004301, AC004301 Drosophila melanogaster DNA sequence (P1 D... 40 1.4  
 U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA,... 40 1.4

## HUMAN ESTs

W22160, W22160 63A6 Human retina cDNA Tsp509I-cleaved sublibr... 791 0.0  
 AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0  
 AA348243, AA348243 EST54707 Hippocampus I Homo sapiens cDNA 5... 513 e-143  
 AA551799, AA551799 nk04a11.s1 NCI\_CGAP\_Co2 Homo sapiens cDNA ... 363 4e-98  
 AA327309, AA327309 EST30621 Colon I Homo sapiens cDNA 5' end 353 3e-95  
 AA344913, AA344913 EST50856 Gall bladder II Homo sapiens cDNA... 337 2e-90  
 AA121174, AA121174 zl88g08.s1 Stratagene colon (#937204) Homo... 317 2e-84  
 AA121198, AA121198 zl88g08.r1 Stratagene colon (#937204) Homo... 317 2e-84  
 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR Homo sapie... 42 0.17  
 AA888147, AA888147 04h11.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 40 0.67  
 AA946650, AA946650 oq38h09.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.67  
 AA435587, AA435587 zt85d07.s1 Soares testis NHT Homo sapiens ... 40 0.67  
 AA806381, AA806381 oc22g05.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.67  
 AA577174, AA577174 nm86e11.s1 NCI\_CGAP\_Co9 Homo sapiens cDNA ... 40 0.67  
 AA215903, AA215903 hp0042.seq.F Fetal heart, Lambda ZAP Expre... 40 0.67  
 AA262229, AA262229 zs25b12.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.67  
 AA969632, AA969632 op38h05.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 40 0.67  
 N35888, N35888 yy28b05.s1 Homo sapiens cDNA clone 272529 3'. 40 0.67  
 AI005324, AI005324 ou13h07.x1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 40 0.67  
 AA172158, AA172158 zp29a01.s1 Stratagene neuroepithelium (#93... 40 0.67  
 AA860208, AA860208 ak48c10.s1 Soares testis NHT Homo sapiens ... 40 0.67  
 AA814296, AA814296 nz07d08.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.67  
 AA873216, AA873216 oh70f04.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.67  
 AA403143, AA403143 zv66d01.r1 Soares total fetus Nb2HF8 9w Ho... 40 0.67  
 W45005, W45005 zc05c12.r1 Soares parathyroid tumor NbHPA Homo... 40 0.67  
 W32428, W32428 zc05c12.s1 Soares parathyroid tumor NbHPA Homo... 40 0.67  
 AA974988, AA974988 on59b06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 40 0.67  
 AA725024, AA725024 ah97h10.s1 Soares NFL T GBC S1 Homo sapien... 40 0.67  
 AA757360, AA757360 ah98a01.s1 Soares NFL T GBC S1 Homo sapien... 40 0.67  
 N72025, N72025 yz96g02.s1 Homo sapiens cDNA clone 290930 3'. 40 0.67  
 R02514, R02514 ye70b08.r1 Homo sapiens cDNA clone 123063 5'. 40 0.67  
 AA039536, AA039536 zk39h10.s1 Soares pregnant uterus NbHPU Ho... 40 0.67  
 AA877455, AA877455 ob33g01.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.67  
 AA041240, AA041240 zf07g05.r1 Soares fetal heart NbHH19W Homo... 40 0.67

AA903406, AA903406 ok62c11.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 40 0.67  
 AA461270, AA461270 zx63b07.r1 Soares total fetus Nb2HF8 9w Ho... 40 0.67  
 AA927863, AA927863 om18a08.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 40 0.67  
 AA587486, AA587486 nn84e09.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 40 0.67  
 W47466, W47466 zc34h02.r1 Soares senescent fibroblasts NbHSF ... 40 0.67  
 AA022495, AA022495 ze70e04.s1 Soares fetal heart NbHH19W Homo... 40 0.67  
 AA460961, AA460961 zx63b07.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.67  
 AA393904, AA393904 zt85e06.r1 Soares testis NHT Homo sapiens ... 40 0.67  
 AA872272, AA872272 oh72a11.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.67  
 W47341, W47341 zc34h02.s1 Soares senescent fibroblasts NbHSF ... 40 0.67  
 N72024, N72024 yz96g01.s1 Homo sapiens cDNA clone 290928 3'. 40 0.67  
 N35076, N35076 yy19b08.s1 Homo sapiens cDNA clone 271671 3'. 40 0.67  
 AA813115, AA813115 aj44d06.s1 Soares testis NHT Homo sapiens ... 40 0.67  
 AA826741, AA826741 85f12.s1 NCI\_CGAP\_Pr24 Homo sapiens cDNA... 40 0.67  
 AA160827, AA160827 zo62e01.s1 Stratagene pancreas (#937208) H... 40 0.67  
 AI040354, AI040354 oy33d12.x1 Soares\_parathyroid\_tumor\_NbHPA ... 40 0.67  
 AA573297, AA573297 nk98d09.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.67  
 AA416559, AA416559 zu18c03.r1 Soares NhHMPu S1 Homo sapiens c... 40 0.67  
 AA401079, AA401079 zv66d01.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.67  
 AI005204, AI005204 ou60c12.x1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 40 0.67  
 N21678, N21678 yx63g01.s1 Soares melanocyte 2NbHM Homo sapien... 40 0.67  
 AA824270, AA824270 aj29f01.s1 Soares testis NHT Homo sapiens ... 40 0.67  
 AA804907, AA804907 oa89a01.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.67  
 AA759038, AA759038 ah75h11.s1 Soares testis NHT Homo sapiens ... 40 0.67  
 AA417295, AA417295 zu18c03.s1 Soares NhHMPu S1 Homo sapiens c... 40 0.67  
 AA628544, AA628544 af27h12.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.67  
 AA618498, AA618498 np30a11.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 40 0.67  
 AA503727, AA503727 ne49g02.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.67  
 AA514777, AA514777 ni24b01.s1 NCI\_CGAP\_Co4 Homo sapiens cDNA ... 40 0.67  
 AA040802, AA040802 zf07g05.s1 Soares fetal heart NbHH19W Homo... 40 0.67  
 AA770473, AA770473 ah89h06.s1 Soares NFL T GBC S1 Homo sapien... 40 0.67  
 AA759377, AA759377 ah54a10.s1 Soares testis NHT Homo sapiens ... 40 0.67  
 AA629243, AA629243 zu77e03.s1 Soares testis NHT Homo sapiens ... 40 0.67  
 AA262162, AA262162 zs25b12.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.67  
 AA161105, AA161105 zo58c05.s1 Stratagene pancreas (#937208) H... 38 2.6  
 AA852281, AA852281 NHTBCae11g05r1 Normal Human Trabecular Bon... 38 2.6  
 AA948291, AA948291 oq34d02.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 38 2.6  
 AA416734, AA416734 zu08c01.s1 Soares testis NHT Homo sapiens ... 38 2.6  
 N98472, N98472 yy65a04.r1 Homo sapiens cDNA clone 278382 5'. 38 2.6  
 AA416815, AA416815 zu08c01.r1 Soares testis NHT Homo sapiens ... 38 2.6  
 AA431486, AA431486 zw72g01.s1 Soares testis NHT Homo sapiens ... 38 2.6  
 H30248, H30248 yp42a01.s1 Homo sapiens cDNA clone 190056 3'. 38 2.6  
 R82551, R82551 yj19d06.r1 Homo sapiens cDNA clone 149195 5'. 38 2.6

AA616807, AA616807 vn68c05.r1 Barstead mouse irradiated colon... 180 1e-43  
 AA014223, AA014223 mh20a03.r1 Soares mouse placenta 4NbMP13.5... 40 0.24  
 AA014768, AA014768 mi66h04.r1 Soares mouse embryo NbME13.5 14... 40 0.24  
 AA185487, AA185487 mt62c07.r1 Soares 2NbMT Mus musculus cDNA ... 40 0.24  
 AA103139, AA103139 mo17f05.r1 Life Tech mouse embryo 13 5dpc ... 40 0.24  
 AI048515, AI048515 uh61e08.r1 Soares mouse embryonic stem cel... 40 0.24  
 AA711859, AA711859 vu59c10.r1 Soares mouse mammary gland NbMM... 40 0.24  
 AA009071, AA009071 mg87b11.r1 Soares mouse embryo NbME13.5 14... 40 0.24  
 AA276740, AA276740 vc42a12.r1 Soares mouse 3NbMS Mus musculus... 40 0.24  
 AA497479, AA497479 vh29b12.r1 Soares mouse mammary gland NbMM... 40 0.24  
 AA038869, AA038869 mi95b10.r1 Soares mouse p3NMF19.5 Mus musc... 40 0.24  
 AA790448, AA790448 vw04f09.r1 Soares mouse mammary gland NbMM... 40 0.24  
 AA881111, AA881111 vz06e09.r1 Soares mouse mammary gland NbMM... 40 0.24  
 AA007762, AA007762 mg76b03.r1 Soares mouse embryo NbME13.5 14... 40 0.24  
 W83172, W83172 mf09a06.r1 Soares mouse p3NMF19.5 Mus musculus... 40 0.24  
 AA106439, AA106439 ml59a08.r1 Stratagene mouse testis (#93730... 40 0.24  
 AA000268, AA000268 mg32e09.r1 Soares mouse embryo NbME13.5 14... 40 0.24  
 AI047077, AI047077 uh61g06.r1 Soares mouse embryonic stem cel... 40 0.24  
 AA543280, AA543280 vj80h05.r1 Soares mouse mammary gland NbMM... 40 0.24  
 AA106301, AA106301 ml81a09.r1 Stratagene mouse kidney (#93731... 40 0.24  
 AA467482, AA467482 ve01a10.r1 Soares mouse NbMH Mus musculus ... 40 0.24  
 AA797372, AA797372 vw27b08.r1 Soares mouse mammary gland NbMM... 40 0.24  
 W77724, W77724 me84h06.r1 Soares mouse embryo NbME13.5 14.5 M... 40 0.24  
 AA049011, AA049011 mj48c09.r1 Soares mouse embryo NbME13.5 14... 40 0.24  
 AA763419, AA763419 vw54a12.r1 Soares mouse mammary gland NMLM... 40 0.24  
 AA138067, AA138067 mq37c11.r1 Barstead MPLRB1 Mus musculus cD... 40 0.24  
 AA475425, AA475425 vh20g09.r1 Soares mouse mammary gland NbMM... 40 0.24  
 AA469884, AA469884 vf71g10.r1 Barstead mouse pooled organs MP... 40 0.24  
 AA016868, AA016868 mh36e12.r1 Soares mouse placenta 4NbMP13.5... 40 0.24  
 AA230758, AA230758 my32g10.r1 Barstead mouse pooled organs MP... 40 0.24  
 AA833479, AA833479 uc91c03.r1 Soares mouse uterus NMPu Mus mu... 40 0.24  
 W61547, W61547 md57a02.r1 Soares mouse embryo NbME13.5 14.5 M... 40 0.24  
 AA033481, AA033481 mi42b07.r1 Soares mouse embryo NbME13.5 14... 40 0.24  
 AA068686, AA068686 mm59a03.r1 Stratagene mouse embryonic carc... 38 0.94  
 AA796056, AA796056 vo65d01.r1 Soares mouse mammary gland NbMM... 36 3.7  
 C87249, C87249 Mus musculus fertilized egg cDNA 3'-end seque... 36 3.7  
 AA921560, AA921560 vy52c06.r1 Stratagene mouse lung 937302 Mu... 36 3.7  
 W87202, W87202 mf55g08.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.7  
 AA542324, AA542324 vk53e07.r1 Stratagene mouse Tcell 937311 M... 36 3.7  
 AA967316, AA967316 vj47a03.r1 Stratagene mouse skin (#937313)... 36 3.7  
 W62989, W62989 md88h12.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.7  
 AA530735, AA530735 vj32g11.r1 Stratagene mouse diaphragm (#93... 36 3.7  
 AA218431, AA218431 my07e05.r1 Barstead mouse lung MPLRB2 Mus ... 36 3.7  
 AA591243, AA591243 vm18c04.r1 Knowles Solter mouse blastocyst... 36 3.7

AI047609, AI047609 uh63g07.r1 Soares mouse embryonic stem cel... 36 3.7  
 AA692425, AA692425 vt59b05.r1 Barstead mouse irradiated colon... 36 3.7  
 AA966976, AA966976 ua38f11.r1 Soares mouse mammary gland NbMM... 36 3.7  
 AA856298, AA856298 vw99b01.r1 Soares 2NbMT Mus musculus cDNA ... 36 3.7  
 W20935, W20935 mb96c07.r1 Soares mouse p3NMF19.5 Mus musculus... 36 3.7  
 AA230661, AA230661 mw15f08.r1 Soares mouse 3NME12 5 Mus muscu... 36 3.7  
 AA111190, AA111190 mp66b11.r1 Soares 2NbMT Mus musculus cDNA ... 36 3.7  
 AA840087, AA840087 uc99h12.r1 Soares mouse uterus NMPu Mus mu... 36 3.7  
 AA089210, AA089210 mo05d10.r1 Stratagene mouse lung 937302 Mu... 36 3.7  
 AI035925, AI035925 ub49e05.r1 Soares mouse mammary gland NbMM... 36 3.7  
 AA824205, AA824205 vy20g08.r1 Stratagene mouse macrophage (#9... 36 3.7  
 AA793845, AA793845 vr35e12.r1 Barstead mouse myotubes MPLRB5 ... 36 3.7  
 AA239210, AA239210 mx89e02.r1 Soares mouse NML Mus musculus c... 36 3.7  
 AA711873, AA711873 vu28e06.r1 Barstead mouse myotubes MPLRB5 ... 36 3.7  
 AA645119, AA645119 vs72d03.r1 Stratagene mouse skin (#937313)... 36 3.7

AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... 42 0.053  
 C83463, C83463 Oryctolagus cuniculus corneal endothelial cDN... 38 0.84  
 AA859448, AA859448 UI-R-A0-bf-b-01-0-UI.s1 UI-R-A0 Rattus nor... 38 0.84  
 AA874930, AA874930 UI-R-E0-ci-b-05-0-UI.s1 UI-R-E0 Rattus nor... 38 0.84  
 C82607, C82607 Oryctolagus cuniculus corneal endothelial cDN... 38 0.84  
 AI009631, AI009631 EST204082 Normalized rat lung, Bento Soare... 38 0.84  
 AA801145, AA801145 EST190642 Normalized rat ovary, Bento Soar... 38 0.84  
 AI012760, AI012760 EST207211 Normalized rat placenta, Bento S... 38 0.84  
 AA956139, AA956139 UI-R-E1-fi-h-08-0-UI.s1 UI-R-E1 Rattus nor... 38 0.84  
 AA801144, AA801144 EST190641 Normalized rat ovary, Bento Soar... 38 0.84  
 AA660819, AA660819 00713 MtrHE Medicago truncatula cDNA 5' ... 38 0.84  
 AA859865, AA859865 UI-R-E0-cc-b-04-0-UI.s1 UI-R-E0 Rattus nor... 38 0.84  
 AI009035, AI009035 EST203486 Normalized rat embryo, Bento Soa... 38 0.84  
 AA859542, AA859542 UI-R-E0-br-d-03-0-UI.s1 UI-R-E0 Rattus nor... 38 0.84  
 T00613, T00613 wEST01334 Caenorhabditis elegans cDNA clone CE... 38 0.84  
 H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp... 36 3.3  
 AA125602, AA125602 JM00M011.QM3 Miracidia Sjc 3/96 Schistosom... 36 3.3  
 D45997, RICS10346A Rice cDNA, partial sequence (S10346\_1A). 36 3.3  
 AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 3.3  
 C68472, C68472 C.elegans cDNA clone yk305a12 : 5' end, singl... 36 3.3  
 AA785775, AA785775 h4b05a1.f1 Aspergillus nidulans 24hr asexu... 36 3.3  
 D46069, RICS10475A Rice cDNA, partial sequence (S10475\_1A). 36 3.3  
 AA660859, AA660859 00754 MtrHE Medicago truncatula cDNA 5' si... 36 3.3  
 Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... 36 3.3  
 Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... 36 3.3  
 AA955567, AA955567 UI-R-E1-fa-a-08-0-UI.s1 UI-R-E1 Rattus nor... 36 3.3  
 AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... 36 3.3  
 Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 3.3

SEO ID NO:548

U66197, HSU66197	Human fibroblast growth factor homologous fa...	42	0.34
AF020738, AF020738	Mus musculus fibroblast growth factor-rela...	42	0.34
U66201, MMU66201	Mus musculus fibroblast growth factor homolo...	42	0.34
Z46966, MMIMOGN44	M.musculus mRNA for imogen 44.	40	1.3
AC004301, AC004301	Drosophila melanogaster DNA sequence (P1 D...	40	1.3
U86662, LEU86662	Lycopersicon esculentum VPS41 (tVPS41) mRNA,...	40	1.3
U85773, HSU85773	Human phosphomannomutase (PMM2) mRNA, comple...	40	1.3

## HUMAN ESTs

W22160, W22160	63A6 Human retina cDNA Tsp509I-cleaved sublibr...	791	0.0
AA860926, AA860926	ak22d06.s1 Soares testis NHT Homo sapiens ...	650	0.0
AA348243, AA348243	EST54707 Hippocampus I Homo sapiens cDNA 5...	513	e-143
AA551799, AA551799	nk04a11.s1 NCI_CGAP_Co2 Homo sapiens cDNA ...	363	3e-98
AA327309, AA327309	EST30621 Colon I Homo sapiens cDNA 5' end	353	3e-95
AA344913, AA344913	EST50856 Gall bladder II Homo sapiens cDNA...	337	2e-90
AA121198, AA121198	zl88g08.r1 Stratagene colon (#937204) Homo...	317	2e-84
AA121174, AA121174	zl88g08.s1 Stratagene colon (#937204) Homo...	317	2e-84
AA001561, AA001561	ze46e07.s1 Soares retina N2b4HR Homo sapie...	42	0.16
AA041240, AA041240	zf07g05.r1 Soares fetal heart NbHH19W Homo...	40	0.64
AA039536, AA039536	zk39h10.s1 Soares pregnant uterus NbHPU Ho...	40	0.64
AA040802, AA040802	zf07g05.s1 Soares fetal heart NbHH19W Homo...	40	0.64
AA573297, AA573297	nk98d09.s1 NCI_CGAP_Co3 Homo sapiens cDNA ...	40	0.64
N35888, N35888	yy28b05.s1 Homo sapiens cDNA clone 272529 3'.	40	0.64
AA888147, AA888147	04h11.s1 NCI_CGAP_Co10 Homo sapiens cDNA...	40	0.64
AA172158, AA172158	zp29a01.s1 Stratagene neuroepithelium (#93...	40	0.64
AA877455, AA877455	ob33g01.s1 NCI_CGAP_Kid5 Homo sapiens cDNA...	40	0.64
R02514, R02514	ye70b08.r1 Homo sapiens cDNA clone 123063 5'.	40	0.64
AA514777, AA514777	ni24b01.s1 NCI_CGAP_Co4 Homo sapiens cDNA ...	40	0.64
AA416734, AA416734	zu08c01.s1 Soares testis NHT Homo sapiens ...	38	2.5
N98472, N98472	yy65a04.r1 Homo sapiens cDNA clone 278382 5'.	38	2.5
AA416815, AA416815	zu08c01.r1 Soares testis NHT Homo sapiens ...	38	2.5
AA431486, AA431486	zw72g01.s1 Soares testis NHT Homo sapiens ...	38	2.5
AA948291, AA948291	oq34d02.s1 NCI_CGAP_GC4 Homo sapiens cDNA ...	38	2.5
AA852281, AA852281	NHTBCae11g05r1 Normal Human Trabecular Bon...	38	2.5

[illegible]

AA616807, AA616807	vn68c05.r1	Barstead mouse irradiated colon...	180	1e-43
AA469884, AA469884	vf71g10.r1	Barstead mouse pooled organs MP...	40	0.23
AA230758, AA230758	my32g10.r1	Barstead mouse pooled organs MP...	40	0.23
AA038869, AA038869	mi95b10.r1	Soares mouse p3NMF19.5 Mus musc...	40	0.23
AA763419, AA763419	vw54a12.r1	Soares mouse mammary gland NMLM...	40	0.23
AA185487, AA185487	mt62c07.r1	Soares 2NbMT Mus musculus cDNA ...	40	0.23
AA106439, AA106439	ml59a08.r1	Stratagene mouse testis (#93730...	40	0.23
AA276740, AA276740	vc42a12.r1	Soares mouse 3NbMS Mus musculus...	40	0.23
AA068686, AA068686	mm59a03.r1	Stratagene mouse embryonic carc...	38	0.91
AA711873, AA711873	vu28e06.r1	Barstead mouse myotubes MPLRB5 ...	36	3.6
AA856298, AA856298	vw99b01.r1	Soares 2NbMT Mus musculus cDNA ...	36	3.6
W20935, W20935	mb96c07.r1	Soares mouse p3NMF19.5 Mus musculus...	36	3.6
AA966976, AA966976	ua38f11.r1	Soares mouse mammary gland NbMM...	36	3.6
AA921560, AA921560	vy52c06.r1	Stratagene mouse lung 937302 Mu...	36	3.6
AA692425, AA692425	vt59b05.r1	Barstead mouse irradiated colon...	36	3.6
W87202, W87202	mf55g08.r1	Soares mouse embryo NbME13.5 14.5 M...	36	3.6
AA840087, AA840087	uc99h12.r1	Soares mouse uterus NMPu Mus mu...	36	3.6
AA111190, AA111190	mp66b11.r1	Soares 2NbMT Mus musculus cDNA ...	36	3.6
AA239210, AA239210	mx89e02.r1	Soares mouse NML Mus musculus c...	36	3.6
AA793845, AA793845	vr35e12.r1	Barstead mouse myotubes MPLRB5 ...	36	3.6
AA645119, AA645119	vs72d03.r1	Stratagene mouse skin (#937313)...	36	3.6
AA230661, AA230661	mw15f08.r1	Soares mouse 3NME12 5 Mus muscu...	36	3.6
AA824205, AA824205	vy20g08.r1	Stratagene mouse macrophage (#9...	36	3.6
C87249, C87249		Mus musculus fertilized egg cDNA 3'-end seque...	36	3.6
AA967316, AA967316	vj47a03.r1	Stratagene mouse skin (#937313)...	36	3.6
AA591243, AA591243	vm18c04.r1	Knowles Solter mouse blastocyst...	36	3.6
AI035925, AI035925	ub49e05.r1	Soares mouse mammary gland NbMM...	36	3.6
AA530735, AA530735	vj32g11.r1	Stratagene mouse diaphragm (#93...	36	3.6
AA218431, AA218431	my07e05.r1	Barstead mouse lung MPLRB2 Mus ...	36	3.6
W62989, W62989	md88h12.r1	Soares mouse embryo NbME13.5 14.5 M...	36	3.6
AA089210, AA089210	mo05d10.r1	Stratagene mouse lung 937302 Mu...	36	3.6
AA796056, AA796056	vo65d01.r1	Soares mouse mammary gland NbMM...	36	3.6
AA542324, AA542324	vk53e07.r1	Stratagene mouse Tcell 937311 M...	36	3.6

AA957268, AA957268	UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor...	42	0.052
T00613, T00613	wEST01334 Caenorhabditis elegans cDNA clone CE...	38	0.81
AA660819, AA660819	00713 MtRHE Medicago truncatula cDNA 5'	38	0.81
AA956139, AA956139	UI-R-E1-fi-h-08-0-UI.s1 UI-R-E1 Rattus nor...	38	0.81
D46069, RICS10475A	Rice cDNA, partial sequence (S10475_1A).	36	3.2
AA842765, AA842765	M-EST080 Sugarcane mature stalk Saccharum ...	36	3.2
AA955567, AA955567	UI-R-E1-fa-a-08-0-UI.s1 UI-R-E1 Rattus nor...	36	3.2
Z33974, ATTS3035	A. thaliana transcribed sequence; clone PAP...	36	3.2
H32878, H32878	EST108396 Rat PC-12 cells, untreated Rattus sp...	36	3.2
AA660859, AA660859	00754 MtRHE Medicago truncatula cDNA 5' si...	36	3.2

D45997, RICS10346A Rice cDNA, partial sequence (S10346\_1A). 36 3.2  
 Z32603, ATTS2731 *A. thaliana* transcribed sequence; clone PAP... 36 3.2  
 AA785775, AA785775 h4b05a1.f1 *Aspergillus nidulans* 24hr asexu... 36 3.2  
 C68472, C68472 *C.elegans* cDNA clone yk305a12 : 5' end, singl... 36 3.2  
 AA125602, AA125602 JM00M011.QM3 *Miracidia Sjc* 3/96 *Schistosom*... 36 3.2  
 AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 3.2  
 Z32602, ATTS2730 *A. thaliana* transcribed sequence; clone PAP... 36 3.2

SEQ ID NO:549

U79271, HSU79271 Human clones 23920 and 23921 mRNA sequence 650 0.0  
 AC000395, AC000395 Genomic sequence from Human 9q34, complete... 42 0.28  
 AC004636, AC004636 *Homo sapiens* chromosome 5, P1 clone 1268h6... 42 0.28  
 M94579, HUMCEL Human carboxyl ester lipase (CEL) gene, comple... 42 0.28  
 AC002097, AC002097 *Homo sapiens* chromosome 9q34, clone 246H5,... 42 0.28  
 AB006709, AB006709 *Vibrio alginolyticus* rpoN gene for RNA po... 42 0.28  
 Z47074, CEK07C10 *Caenorhabditis elegans* cosmid K07C10, compl... 40 1.1  
 AC004755, AC004755 *Homo sapiens* chromosome 19, fosmid 37502, ... 40 1.1  
 Z28051, SCYKL051W *S.cerevisiae* chromosome XI reading frame O... 40 1.1  
 AF022655, AF022655 *Homo sapiens* cep250 centrosome associated ... 40 1.1  
 AB006708, AB006708 *Arabidopsis thaliana* genomic DNA, chromos... 40 1.1  
 AF049105, AF049105 *Homo sapiens* centrosomal Nek2-associated p... 40 1.1  
 Z28050, SCYKL050C *S.cerevisiae* chromosome XI reading frame O... 40 1.1  
 X75781, SCXI286K *S.cerevisiae* chromosome XI (28.6 kb) DNA fo... 40 1.1  
 Y16899, DMY16899 *Drosophila melanogaster* mRNA for optomotor-... 38 4.3  
 M87854, RATBARK1 *Rattus norvegicus* beta-adrenergic receptor k... 38 4.3  
 M74822, RATMHTLL Rat MHC class I TL-like protein gene, comple... 38 4.3  
 M80776, HUMBARK1A Human beta-adrenergic receptor kinase 1 mRN... 38 4.3  
 D84549, YSACA *Candida tropicalis* DNA for carnitine acetyltra... 38 4.3  
 L23127, RATRMCI *Rattus norvegicus* germline MHC class I gene, ... 38 4.3  
 AC004257, AC004257 *Homo sapiens* chromosome 19, cosmid R33209,... 38 4.3  
 U70850, CELF28F9 *Caenorhabditis elegans* cosmid F28F9 38 4.3  
 U88309, CELT23B3 *Caenorhabditis elegans* cosmid T23B3 38 4.3  
 X53421, DVCHOS18 *D. virilis* s18, s15, s19, s16 chorion prote... 38 4.3  
 D89245, D89245 *Schizosaccharomyces pombe* mRNA, partial cds, ... 38 4.3  
 AF009623, AF009623 *Parascaris univalens* PUMA1 (puma1) mRNA, c... 38 4.3  
 S48813, S48813 beta-adrenergic receptor kinase [rats, brain, ... 38 4.3  
 Z67883, CEK02A4 *Caenorhabditis elegans* cosmid K02A4, complet... 38 4.3  
 U90567, GGU90567 *Gallus gallus* glutamine rich protein mRNA, p... 38 4.3  
 M98498, BOVEZRINA *Bos taurus* ezrin mRNA, complete cds. 38 4.3  
 M34073, MUSMHT10C *Mus musculus* (clone T10-c) MHC class I cell... 38 4.3

002090 62629160



S81843, S81843 beta-adrenergic receptor kinase 1 [Syrian hams... 38 4.3  
 X61157, HSBARK H.sapiens mRNA for beta-adrenergic receptor k... 38 4.3  
 U08438, HSNBARKS4 Human beta-adrenergic receptor kinase (ADRB... 38 4.3  
 U39674, CELC06E2 Caenorhabditis elegans cosmid C06E2. 38 4.3

# HUMAN ESTs

W29097, W29097 56d11 Human retina cDNA randomly primed sublib... 1045 0.0  
 AA886109, AA886109 ny44f05.s1 NCI\_CGAP\_Pr12 Homo sapiens cDNA... 656 0.0  
 AA829894, AA829894 oe51e12.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 650 0.0  
 AA879456, AA879456 oj91g03.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 650 0.0  
 AA029201, AA029201 zk12f08.s1 Soares pregnant uterus NbHPU Ho... 650 0.0  
 AA102109, AA102109 zk87g11.s1 Soares pregnant uterus NbHPU Ho... 650 0.0  
 AA843811, AA843811 ak09c08.s1 Soares parathyroid tumor NbHPA ... 650 0.0  
 W72147, W72147 zd70f08.s1 Soares fetal heart NbHH19W Homo sap... 650 0.0  
 N51485, N51485 yz04e06.s1 Homo sapiens cDNA clone 282082 3'. 650 0.0  
 AI033069, AI033069 ow93f02.s1 Soares\_fetal\_liver\_spleen\_1NFLS... 642 0.0  
 AA161465, AA161465 zo73a06.s1 Stratagene pancreas (#937208) H... 638 0.0  
 N51277, N51277 yz14d07.s1 Homo sapiens cDNA clone 283021 3'. 636 e-180  
 N64528, N64528 yz91e06.s1 Homo sapiens cDNA clone 290434 3'. 636 e-180  
 H99906, H99906 yx32h10.s1 Homo sapiens cDNA clone 263491 3'. 636 e-180  
 AA812519, AA812519 ai79b03.s1 Soares testis NHT Homo sapiens ... 636 e-180  
 R71679, R71679 yj85e08.s1 Homo sapiens cDNA clone 155558 3'. 628 e-178  
 AA744290, AA744290 ny51d02.s1 NCI\_CGAP\_Pr18 Homo sapiens cDNA... 626 e-177  
 AI038590, AI038590 ox34e03.s1 Soares\_total\_fetus\_Nb2HF8\_9w Ho... 624 e-177  
 AA099913, AA099913 zk87g11.r1 Soares pregnant uterus NbHPU Ho... 624 e-177  
 AA083859, AA083859 zn16d06.s1 Stratagene neuroepithelium NT2R... 622 e-176  
 AA883684, AA883684 al58a05.s1 Soares NFL T GBC S1 Homo sapien... 613 e-173  
 R39448, R39448 yc95d03.s1 Homo sapiens cDNA clone 23921 3'. 593 e-167  
 R36854, R36854 yf52c07.s1 Homo sapiens cDNA clone 25899 3'. 591 e-167  
 H98684, H98684 yx17g01.s1 Homo sapiens cDNA clone 262032 3'. 585 e-165  
 R07471, R07471 ye97a06.s1 Homo sapiens cDNA clone 125650 3'. 581 e-164  
 AA910762, AA910762 ol25h06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 559 e-157  
 AA083954, AA083954 zn17d06.s1 Stratagene neuroepithelium NT2R... 555 e-156  
 AA346369, AA346369 EST52776 Fetal heart II Homo sapiens cDNA ... 545 e-153  
 R54092, R54092 yg98d07.s1 Homo sapiens cDNA clone 41818 3'. 539 e-151  
 H09074, H09074 yl97a06.s1 Homo sapiens cDNA clone 46164 3'. 535 e-150  
 N21975, N21975 yw30c10.s1 Homo sapiens cDNA clone 253746 3'. 533 e-149  
 D59844, HUM070E11A Human fetal brain cDNA 3'-end GEN-070E11. 466 e-129  
 H11525, H11525 ym15h07.s1 Homo sapiens cDNA clone 48232 3'. 442 e-122  
 AA971254, AA971254 op73c08.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 442 e-122  
 W77907, W77907 zd70f08.r1 Soares fetal heart NbHH19W Homo sap... 428 e-118  
 AA878973, AA878973 oj26d11.s1 NCI\_CGAP\_Kid3 Homo sapiens cDNA... 389 e-106  
 AA715235, AA715235 nv10g01.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 357 2e-96

AA328928, AA328928 EST32475 Embryo, 12 week I Homo sapiens cD... 355 7e-96  
 AA860455, AA860455 aj80f02.s1 Soares parathyroid tumor NbHPA ... 283 2e-74  
 AA026096, AA026096 ze97a04.r1 Soares fetal heart NbHH19W Homo... 268 1e-69  
 AA026516, AA026516 ze97a04.s1 Soares fetal heart NbHH19W Homo... 172 6e-41  
 T26899, T26899 ESTDIR509 Homo sapiens cDNA clone CDDIR509 3'. 170 2e-40  
 N71178, N71178 yw30c10.r1 Homo sapiens cDNA clone 253746 5'. 165 1e-38  
 AA372290, AA372290 EST84170 Raji cells, cyclohexamide treated... 98 3e-18  
 AI038890, AI038890 ox84g12.x1 Soares\_senescent\_fibroblasts\_Nb... 40 0.53  
 D81647, HUM180D08B Human fetal brain cDNA 5'-end GEN-180D08. 38 2.1  
 AA452630, AA452630 zx33f08.r1 Soares total fetus Nb2HF8 9w Ho... 38 2.1  
 AA682624, AA682624 zi19g01.s1 Soares fetal liver spleen 1NFLS... 38 2.1  
 AA742364, AA742364 ny89c12.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 38 2.1  
 AA907234, AA907234 ol03h08.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 38 2.1  
 T09391, T09391 EST07284 Homo sapiens cDNA clone HIBBT71 5' en... 38 2.1  
 AA161236, AA161236 zo59h07.s1 Stratagene pancreas (#937208) H... 38 2.1  
 AA252941, AA252941 zr50g09.r1 Soares NhHMPu S1 Homo sapiens c... 38 2.1  
 AA252245, AA252245 zr64g07.s1 Soares NhHMPu S1 Homo sapiens c... 38 2.1  
 AA780678, AA780678 ac70h01.s1 Stratagene fetal retina 937202 ... 38 2.1  
 W05501, W05501 za84a12.r1 Soares fetal lung NbHL19W Homo sapi... 38 2.1  
 AI039908, AI039908 ox25f07.x1 Soares\_total\_fetus\_Nb2HF8\_9w Ho... 38 2.1  
 AA280664, AA280664 zs99f09.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 38 2.1  
 AA973566, AA973566 oo46f09.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 38 2.1  
 N27253, N27253 yx17g01.r1 Homo sapiens cDNA clone 262032 5'. 38 2.1  
 AA995707, AA995707 os29c09.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 38 2.1  
 AI016407, AI016407 ot72e09.s1 Soares\_total\_fetus\_Nb2HF8\_9w Ho... 38 2.1  
 N70619, N70619 za84a12.s1 Homo sapiens cDNA clone 299230 3'. 38 2.1  
 AA242923, AA242923 zr64g07.r1 Soares NhHMPu S1 Homo sapiens c... 38 2.1  
 AA938631, AA938631 oo96f07.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 38 2.1  
 AA985290, AA985290 am74g03.s1 Stratagene schizo brain S11 Hom... 38 2.1

AA690806, AA690806 vt25h10.r1 Barstead mouse myotubes MPLRB5 ... 377 e-103  
 AA155014, AA155014 mr99h05.r1 Stratagene mouse embryonic carc... 180 8e-44  
 AA269966, AA269966 va57d06.r1 Soares mouse 3NME12 5 Mus muscu... 172 2e-41  
 AA089195, AA089195 mo05h11.r1 Stratagene mouse lung 937302 Mu... 163 2e-38  
 AA466212, AA466212 vg86g02.r1 Barstead mouse pooled organs MP... 68 8e-10  
 AA423476, AA423476 ve76d07.r1 Soares mouse mammary gland NbMM... 60 2e-07  
 AA597213, AA597213 vo28a05.r1 Barstead mouse irradiated colon... 40 0.19  
 AA396266, AA396266 vb45c01.r1 Soares mouse lymph node NbMLN M... 40 0.19  
 AA967806, AA967806 uh05d06.r1 Soares mouse hypothalamus NMHy ... 38 0.75  
 AA591111, AA591111 vm12c06.r1 Knowles Solter mouse blastocyst... 38 0.75  
 W65797, W65797 me14g02.r1 Soares mouse embryo NbME13.5 14.5 M... 38 0.75  
 AA153891, AA153891 mq56e05.r1 Soares 2NbMT Mus musculus cDNA ... 38 0.75

AI019772, AI019772 ua90h02.r1 Soares mouse mammary gland NbMM... 36 3.0  
 AA472253, AA472253 vh10g05.r1 Soares mouse mammary gland NbMM... 36 3.0  
 AA230895, AA230895 mw14g07.r1 Soares mouse 3NME12 5 Mus muscu... 36 3.0  
 W18052, W18052 mb83g03.r1 Soares mouse p3NMF19.5 Mus musculus... 36 3.0  
 AA797681, AA797681 vx66c12.r1 Stratagene mouse skin (#937313)... 36 3.0  
 W66734, W66734 me26g05.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.0  
 AA968020, AA968020 uh07g01.r1 Soares mouse hypothalamus NMHy ... 36 3.0  
 AA051644, AA051644 mj55d12.r1 Soares mouse embryo NbME13.5 14... 36 3.0  
 AA162797, AA162797 mr29g09.r1 Soares mouse 3NbMS Mus musculus... 36 3.0  
 AA549644, AA549644 vk80f08.s1 Knowles Solter mouse 2 cell Mus... 36 3.0  
 AA273295, AA273295 vc01e01.r1 Soares mouse lymph node NbMLN M... 36 3.0  
 AA048480, AA048480 mj33d08.r1 Soares mouse embryo NbME13.5 14... 36 3.0  
 AA098207, AA098207 mn83d01.r1 Stratagene mouse Tcell 937311 M... 36 3.0  
 AA027381, AA027381 mi05c06.r1 Soares mouse placenta 4NbMP13.5... 36 3.0  
 AA544474, AA544474 vk33h06.r1 Soares mouse mammary gland NbMM... 36 3.0  
 AA416466, AA416466 vd15c09.s1 Knowles Solter mouse 2 cell Mus... 36 3.0  
 AA285999, AA285999 vb88h08.r1 Soares mouse 3NbMS Mus musculus... 36 3.0  
 AA175025, AA175025 ms85f06.r1 Soares mouse 3NbMS Mus musculus... 36 3.0  
 AA544386, AA544386 vk33f06.r1 Soares mouse mammary gland NbMM... 36 3.0  
 AA175557, AA175557 ms96g04.r1 Soares mouse 3NbMS Mus musculus... 36 3.0  
 AA711924, AA711924 vu59f09.r1 Soares mouse mammary gland NbMM... 36 3.0  
 AA734052, AA734052 vv22c10.r1 Stratagene mouse heart (#937316... 36 3.0  
 W53738, W53738 md12a12.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.0  
 AA611837, AA611837 vo82a06.r1 Barstead mouse myotubes MPLRB5 ... 36 3.0  
 AA879531, AA879531 vv96f06.r1 Soares mouse mammary gland NbMM... 36 3.0  
 AA288625, AA288625 vb23g09.r1 Soares mouse 3NbMS Mus musculus... 36 3.0

AA784124, AA784124 d2b06a1.fl Aspergillus nidulans 24hr asexu... 38 0.67  
 AI044911, AI044911 UI-R-C1-kk-e-05-0-UI.s1 UI-R-C1 Rattus nor... 36 2.6  
 AA550452, AA550452 1605m3 gmbPfHB3.1, G. Roman Reddy Plasmodi... 36 2.6  
 F20017, ATTS6056 A. thaliana transcribed sequence; clone TAP... 36 2.6  
 AA786697, AA786697 k5d01a1.fl Aspergillus nidulans 24hr asexu... 36 2.6  
 AA433457, AA433457 SW3ICA2345SK Brugia malayi infective larva... 36 2.6

SEQ ID NO:550

U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.20  
 AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.20  
 U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.20  
 Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 0.80

AC004301, AC004301 *Drosophila melanogaster* DNA sequence (P1 D... 40 0.80  
 U86662, LEU86662 *Lycopersicon esculentum* VPS41 (tVPS41) mRNA,... 40 0.80  
 Y14330, HSY14330 *Homo sapiens* partial mRNA for jagged2 protein 38 3.2  
 AF003521, AF003521 *Homo sapiens* Jagged 2 mRNA, complete cds 38 3.2  
 AF029778, AF029778 *Homo sapiens* Jagged2 (JAG2) mRNA, complete... 38 3.2  
 AF020201, AF020201 *Homo sapiens* Jagged 2 mRNA, complete cds 38 3.2  
 Z71523, SCYNL247W *S.cerevisiae* chromosome XIV reading frame ... 38 3.2  
 AF029779, AF029779 *Homo sapiens* hJAG2.del-E6 (JAG2) mRNA, alt... 38 3.2  
 U70049, RNU70049 *Rattus norvegicus* jagged2 precursor gene, pa... 38 3.2  
 X96722, SCCHXIVL *S.cerevisiae* DNA region from chromosome XIV... 38 3.2  
 AF005938, AF005938 *Cavia porcellus* L-type voltage-dependent c... 38 3.2  
 X78972, SBSTRBF *S.bluesensis* ISP 5564 genes strB and strF 38 3.2  
 X94912, HSPR22 *H.sapiens* Pr22 gene 38 3.2

#### HUMAN ESTs

AA860926, AA860926 ak22d06.s1 Soares testis NHT *Homo sapiens* ... 650 0.0  
 AA348243, AA348243 EST54707 Hippocampus I *Homo sapiens* cDNA 5... 513 e-144  
 AA551799, AA551799 nk04a11.s1 NCI\_CGAP\_Co2 *Homo sapiens* cDNA ... 363 2e-98  
 AA327309, AA327309 EST30621 Colon I *Homo sapiens* cDNA 5' end 353 2e-95  
 AA344913, AA344913 EST50856 Gall bladder II *Homo sapiens* cDNA... 337 1e-90  
 AA121174, AA121174 zl88g08.s1 Stratagene colon (#937204) *Homo*... 317 1e-84  
 AA121198, AA121198 zl88g08.r1 Stratagene colon (#937204) *Homo*... 317 1e-84  
 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR *Homo sapie*... 42 0.098  
 AI005204, AI005204 ou60c12.x1 NCI\_CGAP\_Br2 *Homo sapiens* cDNA ... 40 0.39  
 AA757360, AA757360 ah98a01.s1 Soares NFL T GBC S1 *Homo sapien*... 40 0.39  
 AI005324, AI005324 ou13h07.x1 Soares\_NFL\_T\_GBC\_S1 *Homo sapien*... 40 0.39  
 AA416559, AA416559 zu18c03.r1 Soares NhHMPu S1 *Homo sapiens* c... 40 0.39  
 AA262162, AA262162 zs25b12.r1 NCI\_CGAP\_GCB1 *Homo sapiens* cDNA... 40 0.39  
 AA824270, AA824270 aj29f01.s1 Soares testis NHT *Homo sapiens* ... 40 0.39  
 AA826741, AA826741 85f12.s1 NCI\_CGAP\_Pr24 *Homo sapiens* cDNA... 40 0.39  
 AA813115, AA813115 aj44d06.s1 Soares testis NHT *Homo sapiens* ... 40 0.39  
 AA403143, AA403143 zv66d01.r1 Soares total fetus Nb2HF8 9w Ho... 40 0.39  
 AA725024, AA725024 ah97h10.s1 Soares NFL T GBC S1 *Homo sapien*... 40 0.39  
 AA804907, AA804907 oa89a01.s1 NCI\_CGAP\_GCB1 *Homo sapiens* cDNA... 40 0.39  
 AA628544, AA628544 af27h12.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.39  
 AA618498, AA618498 np30a11.s1 NCI\_CGAP\_Pr22 *Homo sapiens* cDNA... 40 0.39  
 AA503727, AA503727 ne49g02.s1 NCI\_CGAP\_Co3 *Homo sapiens* cDNA ... 40 0.39  
 AA460961, AA460961 zx63b07.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.39  
 AA770473, AA770473 ah89h06.s1 Soares NFL T GBC S1 *Homo sapien*... 40 0.39  
 AA759377, AA759377 ah54a10.s1 Soares testis NHT *Homo sapiens* ... 40 0.39  
 AA629243, AA629243 zu77e03.s1 Soares testis NHT *Homo sapiens* ... 40 0.39  
 AA903406, AA903406 ok62c11.s1 NCI\_CGAP\_GC4 *Homo sapiens* cDNA ... 40 0.39  
 AA215903, AA215903 hp0042.seq.F Fetal heart, Lambda ZAP Expre... 40 0.39

AA160827, AA160827 zo62e01.s1 Stratagene pancreas (#937208) H... 40 0.39  
 AA577174, AA577174 nm86e11.s1 NCI\_CGAP\_Co9 Homo sapiens cDNA ... 40 0.39  
 AA969632, AA969632 op38h05.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 40 0.39  
 N72025, N72025 yz96g02.s1 Homo sapiens cDNA clone 290930 3'. 40 0.39  
 AA974988, AA974988 on59b06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 40 0.39  
 W32428, W32428 zc05c12.s1 Soares parathyroid tumor NbHPA Homo... 40 0.39  
 N21678, N21678 yx63g01.s1 Soares melanocyte 2NbHM Homo sapien... 40 0.39  
 AA860208, AA860208 ak48c10.s1 Soares testis NHT Homo sapiens ... 40 0.39  
 AA814296, AA814296 nz07d08.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.39  
 AA806381, AA806381 oc22g05.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.39  
 AA435587, AA435587 zt85d07.s1 Soares testis NHT Homo sapiens ... 40 0.39  
 W45005, W45005 zc05c12.r1 Soares parathyroid tumor NbHPA Homo... 40 0.39  
 AA393904, AA393904 zt85e06.r1 Soares testis NHT Homo sapiens ... 40 0.39  
 AA759038, AA759038 ah75h11.s1 Soares testis NHT Homo sapiens ... 40 0.39  
 AA927863, AA927863 om18a08.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 40 0.39  
 AA461270, AA461270 zx63b07.r1 Soares total fetus Nb2HF8 9w Ho... 40 0.39  
 AA417295, AA417295 zu18c03.s1 Soares NhHMPu S1 Homo sapiens c... 40 0.39  
 W47466, W47466 zc34h02.r1 Soares senescent fibroblasts NbHSF ... 40 0.39  
 AA262229, AA262229 zs25b12.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.39  
 AA587486, AA587486 nn84e09.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 40 0.39  
 AA401079, AA401079 zv66d01.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.39  
 AA872272, AA872272 oh72a11.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.39  
 W47341, W47341 zc34h02.s1 Soares senescent fibroblasts NbHSF ... 40 0.39  
 N72024, N72024 yz96g01.s1 Homo sapiens cDNA clone 290928 3'. 40 0.39  
 N35076, N35076 yy19b08.s1 Homo sapiens cDNA clone 271671 3'. 40 0.39  
 AI040354, AI040354 oy33d12.x1 Soares\_parathyroid\_tumor\_NbHPA ... 40 0.39  
 AA946650, AA946650 oq38h09.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.39  
 AA022495, AA022495 ze70e04.s1 Soares fetal heart NbHH19W Homo... 40 0.39  
 AA873216, AA873216 oh70f04.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.39  
 R82551, R82551 yj19d06.r1 Homo sapiens cDNA clone 149195 5'. 38 1.5  
 H30248, H30248 yp42a01.s1 Homo sapiens cDNA clone 190056 3'. 38 1.5  
 AA161105, AA161105 zo58c05.s1 Stratagene pancreas (#937208) H... 38 1.5  
 AA948291, AA948291 oq34d02.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 38 1.5  
 AA416734, AA416734 zu08c01.s1 Soares testis NHT Homo sapiens ... 38 1.5  
 AA431486, AA431486 zw72g01.s1 Soares testis NHT Homo sapiens ... 38 1.5  
 AA416815, AA416815 zu08c01.r1 Soares testis NHT Homo sapiens ... 38 1.5

AA616807, AA616807 vn68c05.r1 Barstead mouse irradiated colon... 180 6e-44  
 AA467482, AA467482 ve01a10.r1 Soares mouse NbMH Mus musculus ... 40 0.14  
 AA543280, AA543280 vj80h05.r1 Soares mouse mammary gland NbMM... 40 0.14  
 AA009071, AA009071 mg87b11.r1 Soares mouse embryo NbME13.5 14... 40 0.14  
 AA106439, AA106439 ml59a08.r1 Stratagene mouse testis (#93730... 40 0.14

AA014768, AA014768	mi66h04.r1	Soares mouse embryo NbME13.5 14...	40	0.14
AA881111, AA881111	vz06e09.r1	Soares mouse mammary gland NbMM...	40	0.14
AA049011, AA049011	mj48c09.r1	Soares mouse embryo NbME13.5 14...	40	0.14
AA185487, AA185487	mt62c07.r1	Soares 2NbMT Mus musculus cDNA ...	40	0.14
AA763419, AA763419	vw54a12.r1	Soares mouse mammary gland NMLM...	40	0.14
AA016868, AA016868	mh36e12.r1	Soares mouse placenta 4NbMP13.5...	40	0.14
AA833479, AA833479	uc91c03.r1	Soares mouse uterus NMPu Mus mu...	40	0.14
AA790448, AA790448	vw04f09.r1	Soares mouse mammary gland NbMM...	40	0.14
AA711859, AA711859	vu59c10.r1	Soares mouse mammary gland NbMM...	40	0.14
AA469884, AA469884	vf71g10.r1	Barstead mouse pooled organs MP...	40	0.14
AA230758, AA230758	my32g10.r1	Barstead mouse pooled organs MP...	40	0.14
AA497479, AA497479	vh29b12.r1	Soares mouse mammary gland NbMM...	40	0.14
AA138067, AA138067	mq37c11.r1	Barstead MPLRB1 Mus musculus cD...	40	0.14
AA103139, AA103139	mo17f05.r1	Life Tech mouse embryo 13 5dpc ...	40	0.14
AI047077, AI047077	uh61g06.r1	Soares mouse embryonic stem cel...	40	0.14
AI048515, AI048515	uh61e08.r1	Soares mouse embryonic stem cel...	40	0.14
W61547, W61547	md57a02.r1	Soares mouse embryo NbME13.5 14.5 M...	40	0.14
AA007762, AA007762	mg76b03.r1	Soares mouse embryo NbME13.5 14...	40	0.14
AA000268, AA000268	mg32e09.r1	Soares mouse embryo NbME13.5 14...	40	0.14
AA475425, AA475425	vh20g09.r1	Soares mouse mammary gland NbMM...	40	0.14
AA014223, AA014223	mh20a03.r1	Soares mouse placenta 4NbMP13.5...	40	0.14
AA797372, AA797372	vw27b08.r1	Soares mouse mammary gland NbMM...	40	0.14
AA106301, AA106301	ml81a09.r1	Stratagene mouse kidney (#93731...	40	0.14
AA033481, AA033481	mi42b07.r1	Soares mouse embryo NbME13.5 14...	40	0.14
W77724, W77724	me84h06.r1	Soares mouse embryo NbME13.5 14.5 M...	40	0.14
W83172, W83172	mf09a06.r1	Soares mouse p3NMF19.5 Mus musculus...	40	0.14
AA038869, AA038869	mi95b10.r1	Soares mouse p3NMF19.5 Mus musc...	40	0.14
AA068686, AA068686	mm59a03.r1	Stratagene mouse embryonic carc...	38	0.55
AA111190, AA111190	mp66b11.r1	Soares 2NbMT Mus musculus cDNA ...	36	2.2
AA840087, AA840087	uc99h12.r1	Soares mouse uterus NMPu Mus mu...	36	2.2
AA239210, AA239210	mx89e02.r1	Soares mouse NML Mus musculus c...	36	2.2
AA824205, AA824205	vy20g08.r1	Stratagene mouse macrophage (#9...	36	2.2
C87249, C87249		Mus musculus fertilized egg cDNA 3'-end seque...	36	2.2
AA089210, AA089210	mo05d10.r1	Stratagene mouse lung 937302 Mu...	36	2.2
AA711873, AA711873	vu28e06.r1	Barstead mouse myotubes MPLRB5 ...	36	2.2
AA793845, AA793845	vr35e12.r1	Barstead mouse myotubes MPLRB5 ...	36	2.2
AA645119, AA645119	vs72d03.r1	Stratagene mouse skin (#937313)...	36	2.2
AA967316, AA967316	vj47a03.r1	Stratagene mouse skin (#937313)...	36	2.2
W87202, W87202	mf55g08.r1	Soares mouse embryo NbME13.5 14.5 M...	36	2.2
AA218431, AA218431	my07e05.r1	Barstead mouse lung MPLRB2 Mus ...	36	2.2
AA796056, AA796056	vo65d01.r1	Soares mouse mammary gland NbMM...	36	2.2
AA542324, AA542324	vk53e07.r1	Stratagene mouse Tcell 937311 M...	36	2.2
AA530735, AA530735	vj32g11.r1	Stratagene mouse diaphragm (#93...	36	2.2
AI047609, AI047609	uh63g07.r1	Soares mouse embryonic stem cel...	36	2.2
AA591243, AA591243	vm18c04.r1	Knowles Solter mouse blastocyst...	36	2.2

AA856298, AA856298 vw99b01.r1 Soares 2NbMT Mus musculus cDNA ... 36 2.2  
 AA966976, AA966976 ua38f11.r1 Soares mouse mammary gland NbMM... 36 2.2

AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... 42 0.031  
 AA801145, AA801145 EST190642 Normalized rat ovary, Bento Soar... 38 0.48  
 AI012760, AI012760 EST207211 Normalized rat placenta, Bento S... 38 0.48  
 AA874930, AA874930 UI-R-E0-ci-b-05-0-UI.s1 UI-R-E0 Rattus nor... 38 0.48  
 C82607, C82607 Oryctolagus cuniculus corneal endothelial cDN... 38 0.48  
 AA859865, AA859865 UI-R-E0-cc-b-04-0-UI.s1 UI-R-E0 Rattus nor... 38 0.48  
 C83463, C83463 Oryctolagus cuniculus corneal endothelial cDN... 38 0.48  
 AA801144, AA801144 EST190641 Normalized rat ovary, Bento Soar... 38 0.48  
 AA859448, AA859448 UI-R-A0-bf-b-01-0-UI.s1 UI-R-A0 Rattus nor... 38 0.48  
 AI009631, AI009631 EST204082 Normalized rat lung, Bento Soare... 38 0.48  
 AI009035, AI009035 EST203486 Normalized rat embryo, Bento Soa... 38 0.48  
 AA859542, AA859542 UI-R-E0-br-d-03-0-UI.s1 UI-R-E0 Rattus nor... 38 0.48  
 H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp... 36 1.9  
 AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 1.9  
 Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 1.9  
 Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... 36 1.9  
 Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... 36 1.9  
 AA660859, AA660859 00754 MtrHE Medicago truncatula cDNA 5' si... 36 1.9  
 AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... 36 1.9  
 AA125602, AA125602 JM00M011.QM3 Miracidia Sjc 3/96 Schistosom... 36 1.9  
 AA785775, AA785775 h4b05a1.fl Aspergillus nidulans 24hr asexu... 36 1.9

SEQ ID NO:551

U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.36  
 AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.36  
 U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.36  
 U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA,... 40 1.4  
 U85773, HSU85773 Human phosphomannomutase (PMM2) mRNA, comple... 40 1.4  
 Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 1.4  
 AC004301, AC004301 Drosophila melanogaster DNA sequence (P1 D... 40 1.4

#### HUMAN ESTs

W22160, W22160 63A6 Human retina cDNA Tsp509I-cleaved sublibr... 791 0.0  
 AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0

0046299-050740

AA616807, AA616807	vn68c05.r1	Barstead mouse irradiated colon...	180	1e-43
AA469884, AA469884	vf71g10.r1	Barstead mouse pooled organs MP...	40	0.24
AA038869, AA038869	mi95b10.r1	Soares mouse p3NMF19.5 Mus musc...	40	0.24
AA185487, AA185487	mt62c07.r1	Soares 2NbMT Mus musculus cDNA ...	40	0.24
AA230758, AA230758	my32g10.r1	Barstead mouse pooled organs MP...	40	0.24
AA276740, AA276740	vc42a12.r1	Soares mouse 3NbMS Mus musculus...	40	0.24
AA763419, AA763419	vw54a12.r1	Soares mouse mammary gland NMLM...	40	0.24
AA106439, AA106439	ml59a08.r1	Stratagene mouse testis (#93730...	40	0.24
AA250010, AA250010	mz59b12.r1	Soares mouse lymph node NbMLN M...	38	0.97
AA068686, AA068686	mm59a03.r1	Stratagene mouse embryonic carc...	38	0.97
AA139459, AA139459	mq86a03.r1	Stratagene mouse melanoma (#937...	38	0.97
AA881111, AA881111	vz06e09.r1	Soares mouse mammary gland NbMM...	36	3.8
AA692425, AA692425	vt59b05.r1	Barstead mouse irradiated colon...	36	3.8
AA049011, AA049011	mj48c09.r1	Soares mouse embryo NbME13.5 14...	36	3.8
AA966976, AA966976	ua38f11.r1	Soares mouse mammary gland NbMM...	36	3.8
AI047077, AI047077	uh61g06.r1	Soares mouse embryonic stem cel...	36	3.8
AA103139, AA103139	mo17f05.r1	Life Tech mouse embryo 13 5dpc ...	36	3.8



AA840087, AA840087 uc99h12.r1 Soares mouse uterus NMPu Mus mu... 36 3.8  
 AA543280, AA543280 vj80h05.r1 Soares mouse mammary gland NbMM... 36 3.8  
 AA007762, AA007762 mg76b03.r1 Soares mouse embryo NbME13.5 14... 36 3.8  
 AA014223, AA014223 mh20a03.r1 Soares mouse placenta 4NbMP13.5... 36 3.8  
 AA591243, AA591243 vm18c04.r1 Knowles Solter mouse blastocyst... 36 3.8  
 AA921560, AA921560 vy52c06.r1 Stratagene mouse lung 937302 Mu... 36 3.8  
 W20935, W20935 mb96c07.r1 Soares mouse p3NMF19.5 Mus musculus... 36 3.8  
 AA793845, AA793845 vr35e12.r1 Barstead mouse myotubes MPLRB5 ... 36 3.8  
 AA856298, AA856298 vw99b01.r1 Soares 2NbMT Mus musculus cDNA ... 36 3.8  
 AA833479, AA833479 uc91c03.r1 Soares mouse uterus NMPu Mus mu... 36 3.8  
 AA218431, AA218431 my07e05.r1 Barstead mouse lung MPLRB2 Mus ... 36 3.8  
 AA089210, AA089210 mo05d10.r1 Stratagene mouse lung 937302 Mu... 36 3.8  
 AI047609, AI047609 uh63g07.r1 Soares mouse embryonic stem cel... 36 3.8  
 AA797372, AA797372 vw27b08.r1 Soares mouse mammary gland NbMM... 36 3.8  
 AA138067, AA138067 mq37c11.r1 Barstead MPLRB1 Mus musculus cD... 36 3.8  
 W83172, W83172 mf09a06.r1 Soares mouse p3NMF19.5 Mus musculus... 36 3.8  
 AA542324, AA542324 vk53e07.r1 Stratagene mouse Tcell 937311 M... 36 3.8  
 AA967316, AA967316 vj47a03.r1 Stratagene mouse skin (#937313)... 36 3.8  
 AI035925, AI035925 ub49e05.r1 Soares mouse mammary gland NbMM... 36 3.8  
 AA497479, AA497479 vh29b12.r1 Soares mouse mammary gland NbMM... 36 3.8  
 W87202, W87202 mf55g08.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.8  
 AA016868, AA016868 mh36e12.r1 Soares mouse placenta 4NbMP13.5... 36 3.8  
 AA467482, AA467482 ve01a10.r1 Soares mouse NbMH Mus musculus ... 36 3.8  
 AA014768, AA014768 mi66h04.r1 Soares mouse embryo NbME13.5 14... 36 3.8  
 AA711859, AA711859 vu59c10.r1 Soares mouse mammary gland NbMM... 36 3.8  
 AA530735, AA530735 vj32g11.r1 Stratagene mouse diaphragm (#93... 36 3.8  
 AA009071, AA009071 mg87b11.r1 Soares mouse embryo NbME13.5 14... 36 3.8  
 AA711873, AA711873 vu28e06.r1 Barstead mouse myotubes MPLRB5 ... 36 3.8  
 AA645119, AA645119 vs72d03.r1 Stratagene mouse skin (#937313)... 36 3.8  
 AA106301, AA106301 ml81a09.r1 Stratagene mouse kidney (#93731... 36 3.8  
 AA111190, AA111190 mp66b11.r1 Soares 2NbMT Mus musculus cDNA ... 36 3.8  
 C87249, C87249 Mus musculus fertilized egg cDNA 3'-end seque... 36 3.8  
 AA796056, AA796056 vo65d01.r1 Soares mouse mammary gland NbMM... 36 3.8  
 AA230661, AA230661 mw15f08.r1 Soares mouse 3NME12 5 Mus muscu... 36 3.8  
 AA033481, AA033481 mi42b07.r1 Soares mouse embryo NbME13.5 14... 36 3.8  
 AA000268, AA000268 mg32e09.r1 Soares mouse embryo NbME13.5 14... 36 3.8  
 AI048515, AI048515 uh61e08.r1 Soares mouse embryonic stem cel... 36 3.8  
 W61547, W61547 md57a02.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.8  
 AA790448, AA790448 vw04f09.r1 Soares mouse mammary gland NbMM... 36 3.8  
 AA824205, AA824205 vy20g08.r1 Stratagene mouse macrophage (#9... 36 3.8  
 AA475425, AA475425 vh20g09.r1 Soares mouse mammary gland NbMM... 36 3.8  
 W62989, W62989 md88h12.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.8  
 W77724, W77724 me84h06.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.8  
 AA239210, AA239210 mx89e02.r1 Soares mouse NML Mus musculus c... 36 3.8

AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... 42 0.055  
 AA891284, AA891284 EST195087 Normalized rat heart, Bento Soar... 40 0.22  
 Z83055, RNZ83055 R.norvegicus mRNA; expressed sequence tag; ... 40 0.22  
 AI010967, AI010967 EST205418 Normalized rat muscle, Bento Soa... 40 0.22  
 AA852049, AA852049 EST194818 Normalized rat spleen, Bento Soa... 40 0.22  
 H33489, H33489 EST109542 Rat PC-12 cells, NGF-treated (9 days... 40 0.22  
 AA799616, AA799616 EST189113 Normalized rat heart, Bento Soar... 40 0.22  
 Z83044, RNZ83044 R.norvegicus mRNA; expressed sequence tag; ... 40 0.22  
 AA660819, AA660819 00713 MtrHE Medicago truncatula cDNA 5' 38 0.86  
 AA956139, AA956139 UI-R-E1-fi-h-08-0-UI.s1 UI-R-E1 Rattus nor... 38 0.86  
 T00613, T00613 wEST01334 Caenorhabditis elegans cDNA clone CE... 38 0.86  
 AA785775, AA785775 h4b05a1.f1 Aspergillus nidulans 24hr asexu... 36 3.4  
 AA660859, AA660859 00754 MtrHE Medicago truncatula cDNA 5' si... 36 3.4  
 AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 3.4  
 C68472, C68472 C.elegans cDNA clone yk305a12 : 5' end, singl... 36 3.4  
 AA800635, AA800635 EST190132 Normalized rat lung, Bento Soare... 36 3.4  
 Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 3.4  
 Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... 36 3.4  
 AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... 36 3.4  
 AA955567, AA955567 UI-R-E1-fa-a-08-0-UI.s1 UI-R-E1 Rattus nor... 36 3.4  
 H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp... 36 3.4  
 Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... 36 3.4  
 D45997, RICS10346A Rice cDNA, partial sequence (S10346\_1A). 36 3.4  
 AA125602, AA125602 JM00M011.QM3 Miracidia Sjc 3/96 Schistosom... 36 3.4  
 AA800634, AA800634 EST190131 Normalized rat lung, Bento Soare... 36 3.4  
 D46069, RICS10475A Rice cDNA, partial sequence (S10475\_1A). 36 3.4

SEQ ID NO:552

U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.38  
 AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.38  
 U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.38  
 Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 1.5  
 U86662, LEU86662 Lycopersicon esculentum VPS41 (tvPS41) mRNA,... 40 1.5  
 U85773, HSU85773 Human phosphomannomutase (PMM2) mRNA, comple... 40 1.5

#### HUMAN ESTs

W22160, W22160 63A6 Human retina cDNA Tsp509I-cleaved sublibr... 791 0.0  
 AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0

AA348243, AA348243 EST54707 Hippocampus I Homo sapiens cDNA 5... 513 e-143  
 AA551799, AA551799 nk04a11.s1 NCI\_CGAP\_Co2 Homo sapiens cDNA ... 363 4e-98  
 AA327309, AA327309 EST30621 Colon I Homo sapiens cDNA 5' end 353 4e-95  
 AA344913, AA344913 EST50856 Gall bladder II Homo sapiens cDNA... 337 2e-90  
 AA121198, AA121198 zl88g08.r1 Stratagene colon (#937204) Homo... 317 2e-84  
 AA121174, AA121174 zl88g08.s1 Stratagene colon (#937204) Homo... 317 2e-84  
 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR Homo sapie... 42 0.18  
 AA172158, AA172158 zp29a01.s1 Stratagene neuroepithelium (#93... 40 0.72  
 N35888, N35888 yy28b05.s1 Homo sapiens cDNA clone 272529 3'. 40 0.72  
 AA877455, AA877455 ob33g01.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.72  
 AA573297, AA573297 nk98d09.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.72  
 AA040802, AA040802 zf07g05.s1 Soares fetal heart NbHH19W Homo... 40 0.72  
 R02514, R02514 ye70b08.r1 Homo sapiens cDNA clone 123063 5'. 40 0.72  
 AA514777, AA514777 ni24b01.s1 NCI\_CGAP\_Co4 Homo sapiens cDNA ... 40 0.72  
 AA041240, AA041240 zf07g05.r1 Soares fetal heart NbHH19W Homo... 40 0.72  
 AA888147, AA888147 04h11.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 40 0.72  
 AA039536, AA039536 zk39h10.s1 Soares pregnant uterus NbHPU Ho... 40 0.72  
 AA416734, AA416734 zu08c01.s1 Soares testis NHT Homo sapiens ... 38 2.8  
 N25839, N25839 yx22e05.r1 Homo sapiens cDNA clone 262496 5'. 38 2.8  
 AA431486, AA431486 zw72g01.s1 Soares testis NHT Homo sapiens ... 38 2.8  
 N98472, N98472 yy65a04.r1 Homo sapiens cDNA clone 278382 5'. 38 2.8  
 AA416815, AA416815 zu08c01.r1 Soares testis NHT Homo sapiens ... 38 2.8  
 AA852281, AA852281 NHTBCae11g05r1 Normal Human Trabecular Bon... 38 2.8  
 AA948291, AA948291 oq34d02.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 38 2.8

AA616807, AA616807 vn68c05.r1 Barstead mouse irradiated colon... 180 1e-43  
 AA185487, AA185487 mt62c07.r1 Soares 2NbMT Mus musculus cDNA ... 40 0.26  
 AA276740, AA276740 vc42a12.r1 Soares mouse 3NbMS Mus musculus... 40 0.26  
 AA469884, AA469884 vf71g10.r1 Barstead mouse pooled organs MP... 40 0.26  
 AA230758, AA230758 my32g10.r1 Barstead mouse pooled organs MP... 40 0.26  
 AA038869, AA038869 mi95b10.r1 Soares mouse p3NMF19.5 Mus musc... 40 0.26  
 AA106439, AA106439 ml59a08.r1 Stratagene mouse testis (#93730... 40 0.26  
 AA763419, AA763419 vw54a12.r1 Soares mouse mammary gland NMLM... 40 0.26  
 AA139459, AA139459 mq86a03.r1 Stratagene mouse melanoma (#937... 38 1.0  
 AA068686, AA068686 mm59a03.r1 Stratagene mouse embryonic carc... 38 1.0  
 AA218431, AA218431 my07e05.r1 Barstead mouse lung MPLRB2 Mus ... 36 4.0  
 AI047077, AI047077 uh61g06.r1 Soares mouse embryonic stem cel... 36 4.0  
 C87249, C87249 Mus musculus fertilized egg cDNA 3'-end seque... 36 4.0  
 AI035925, AI035925 ub49e05.r1 Soares mouse mammary gland NbMM... 36 4.0  
 AA111190, AA111190 mp66b11.r1 Soares 2NbMT Mus musculus cDNA ... 36 4.0  
 AA645119, AA645119 vs72d03.r1 Stratagene mouse skin (#937313)... 36 4.0  
 AA530735, AA530735 vj32g11.r1 Stratagene mouse diaphragm (#93... 36 4.0

AA000268, AA000268	mg32e09.r1	Soares mouse embryo NbME13.5 14...	36	4.0
AA793845, AA793845	vr35e12.r1	Barstead mouse myotubes MPLRB5 ...	36	4.0
AA840087, AA840087	uc99h12.r1	Soares mouse uterus NMPu Mus mu...	36	4.0
AA711873, AA711873	vu28e06.r1	Barstead mouse myotubes MPLRB5 ...	36	4.0
AA790448, AA790448	vw04f09.r1	Soares mouse mammary gland NbMM...	36	4.0
AA106301, AA106301	ml81a09.r1	Stratagene mouse kidney (#93731...	36	4.0
AA543280, AA543280	vj80h05.r1	Soares mouse mammary gland NbMM...	36	4.0
AA007762, AA007762	mg76b03.r1	Soares mouse embryo NbME13.5 14...	36	4.0
AA921560, AA921560	vy52c06.r1	Stratagene mouse lung 937302 Mu...	36	4.0
AA692425, AA692425	vt59b05.r1	Barstead mouse irradiated colon...	36	4.0
AA833479, AA833479	uc91c03.r1	Soares mouse uterus NMPu Mus mu...	36	4.0
AA824205, AA824205	vy20g08.r1	Stratagene mouse macrophage (#9...	36	4.0
AA033481, AA033481	mi42b07.r1	Soares mouse embryo NbME13.5 14...	36	4.0
W61547, W61547	md57a02.r1	Soares mouse embryo NbME13.5 14.5 M...	36	4.0
AA796056, AA796056	vo65d01.r1	Soares mouse mammary gland NbMM...	36	4.0
AA467482, AA467482	ve01a10.r1	Soares mouse NbMH Mus musculus ...	36	4.0
AA239210, AA239210	mx89e02.r1	Soares mouse NML Mus musculus c...	36	4.0
AA881111, AA881111	vz06e09.r1	Soares mouse mammary gland NbMM...	36	4.0
AA542324, AA542324	vk53e07.r1	Stratagene mouse Tcell 937311 M...	36	4.0
AA089210, AA089210	mo05d10.r1	Stratagene mouse lung 937302 Mu...	36	4.0
W77724, W77724	me84h06.r1	Soares mouse embryo NbME13.5 14.5 M...	36	4.0
AI048515, AI048515	uh61e08.r1	Soares mouse embryonic stem cel...	36	4.0
AA009071, AA009071	mg87b11.r1	Soares mouse embryo NbME13.5 14...	36	4.0
AA475425, AA475425	vh20g09.r1	Soares mouse mammary gland NbMM...	36	4.0
AA230661, AA230661	mw15f08.r1	Soares mouse 3NME12 5 Mus muscu...	36	4.0
AA138067, AA138067	mq37c11.r1	Barstead MPLRB1 Mus musculus cD...	36	4.0
W83172, W83172	mf09a06.r1	Soares mouse p3NMF19.5 Mus musculus...	36	4.0
AA797372, AA797372	vw27b08.r1	Soares mouse mammary gland NbMM...	36	4.0
AA711859, AA711859	vu59c10.r1	Soares mouse mammary gland NbMM...	36	4.0
AA967316, AA967316	vj47a03.r1	Stratagene mouse skin (#937313)...	36	4.0
W87202, W87202	mf55g08.r1	Soares mouse embryo NbME13.5 14.5 M...	36	4.0
AA103139, AA103139	mo17f05.r1	Life Tech mouse embryo 13 5dpc ...	36	4.0
AA014223, AA014223	mh20a03.r1	Soares mouse placenta 4NbMP13.5...	36	4.0
W62989, W62989	md88h12.r1	Soares mouse embryo NbME13.5 14.5 M...	36	4.0
W20935, W20935	mb96c07.r1	Soares mouse p3NMF19.5 Mus musculus...	36	4.0
AA966976, AA966976	ua38f11.r1	Soares mouse mammary gland NbMM...	36	4.0
AA856298, AA856298	vw99b01.r1	Soares 2NbMT Mus musculus cDNA ...	36	4.0
AA014768, AA014768	mi66h04.r1	Soares mouse embryo NbME13.5 14...	36	4.0
AA497479, AA497479	vh29b12.r1	Soares mouse mammary gland NbMM...	36	4.0
AA049011, AA049011	mj48c09.r1	Soares mouse embryo NbME13.5 14...	36	4.0
AA016868, AA016868	mh36e12.r1	Soares mouse placenta 4NbMP13.5...	36	4.0
AI047609, AI047609	uh63g07.r1	Soares mouse embryonic stem cel...	36	4.0
AA591243, AA591243	vm18c04.r1	Knowles Solter mouse blastocyst...	36	4.0

AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... 42 0.058  
T00613, T00613 wEST01334 Caenorhabditis elegans cDNA clone CE... 38 0.90  
AA956139, AA956139 UI-R-E1-fi-h-08-0-UI.s1 UI-R-E1 Rattus nor... 38 0.90  
AA660819, AA660819 00713 MtRHE Medicago truncatula cDNA 5' 38 0.90  
AA125602, AA125602 JM00M011.QM3 Miracidia Sjc 3/96 Schistosom... 36 3.6  
Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... 36 3.6  
C68472, C68472 C.elegans cDNA clone yk305a12 : 5' end, singl... 36 3.6  
AA785775, AA785775 h4b05a1.f1 Aspergillus nidulans 24hr asexu... 36 3.6  
Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 3.6  
AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 3.6  
Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... 36 3.6  
AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... 36 3.6  
D45997, RICS10346A Rice cDNA, partial sequence (S10346\_1A). 36 3.6  
AA955567, AA955567 UI-R-E1-fa-a-08-0-UI.s1 UI-R-E1 Rattus nor... 36 3.6  
AA800634, AA800634 EST190131 Normalized rat lung, Bento Soare... 36 3.6  
AA660859, AA660859 00754 MtRHE Medicago truncatula cDNA 5' si... 36 3.6  
AA800635, AA800635 EST190132 Normalized rat lung, Bento Soare... 36 3.6  
D46069, RICS10475A Rice cDNA, partial sequence (S10475\_1A). 36 3.6  
H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp... 36 3.6

SEQ ID NO:553

Z99297, HS262D12 Homo sapiens DNA sequence from PAC 262D12 o... 1963 0.0  
Z81540, CEF46B3 Caenorhabditis elegans cosmid F46B3, complet... 40 0.89  
U67488, U67488 Methanococcus jannaschii section 30 of 150 of ... 38 3.5  
AE000786, AE000786 Borrelia burgdorferi plasmid lp28-2, compl... 38 3.5  
L02053, OMMGSHTR1 Ommastrephes sloani glutathione transferase... 38 3.5  
AC004521, ATAC004521 Arabidopsis thaliana chromosome II BAC F... 38 3.5  
L41250, DROGPDHN Drosophila nebulosa glycerol-3-phosphate deh... 38 3.5  
AE000619, HPAE000619 Helicobacter pylori section 97 of 134 of... 38 3.5  
U39720, Mycoplasma genitalium ackA, licA, mucB, rpL10, rpL32... 38 3.5  
AC004533, HUAC004533 Homo sapiens Chromosome 16 BAC clone CIT... 38 3.5  
U62292, HSU62292 Human elastin (ELN) gene, partial cds 38 3.5

#### HUMAN ESTs

W02630, W02630 za52c02.r1 Soares fetal liver spleen 1NFLS Hom... 1009 0.0  
AA557183, AA557183 nl74f12.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 874 0.0  
AA761171, AA761171 nz09e11.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 866 0.0  
AA976975, AA976975 oq26g11.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 854 0.0  
AA449515, AA449515 zx06b11.r1 Soares total fetus Nb2HF8 9w Ho... 848 0.0

002030:66629466

AA678392, AA678392 zi26h10.s1 Soares fetal liver spleen 1NFLS... 848 0.0  
AA909198, AA909198 ol12d06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 831 0.0  
W79208, W79208 zd79g05.r1 Soares fetal heart NbHH19W Homo sap... 813 0.0  
W03125, W03125 za53c02.r1 Soares fetal liver spleen 1NFLS Hom... 807 0.0  
W94750, W94750 ze13h08.r1 Soares fetal heart NbHH19W Homo sap... 785 0.0  
AA354894, AA354894 EST63217 Jurkat T-cells V Homo sapiens cDN... 771 0.0  
H70075, H70075 yr92b03.r1 Homo sapiens cDNA clone 212717 5'. 745 0.0  
W77859, W77859 zd70b08.r1 Soares fetal heart NbHH19W Homo sap... 728 0.0  
AA425424, AA425424 zw48f03.s1 Soares total fetus Nb2HF8 9w Ho... 718 0.0  
AA476893, AA476893 zu29f09.r1 Soares ovary tumor NbHOT Homo s... 688 0.0  
AA456676, AA456676 aa01h02.s1 Soares NhHMPu S1 Homo sapiens c... 688 0.0  
AA662309, AA662309 nu97c11.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 668 0.0  
W72135, W72135 zd70b08.s1 Soares fetal heart NbHH19W Homo sap... 650 0.0  
N74362, N74362 za52c02.s1 Homo sapiens cDNA clone 296162 3'. 622 e-176  
N66917, N66917 za47d09.s1 Homo sapiens cDNA clone 295697 3'. 585 e-165  
AA251287, AA251287 zs04c06.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 583 e-164  
AA971082, AA971082 op70h01.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 567 e-160  
W78165, W78165 zd79g05.s1 Soares fetal heart NbHH19W Homo sap... 565 e-159  
AA253290, AA253290 zr71g03.r1 Soares NhHMPu S1 Homo sapiens c... 559 e-157  
AA729063, AA729063 nw22f08.s1 NCI\_CGAP\_GCB0 Homo sapiens cDNA... 557 e-157  
AA987313, AA987313 or81h06.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 553 e-155  
AA300954, AA300954 EST13832 Testis tumor Homo sapiens cDNA 5'... 541 e-152  
AA425594, AA425594 zw48f03.r1 Soares total fetus Nb2HF8 9w Ho... 529 e-148  
N24014, N24014 yx87g10.s1 Homo sapiens cDNA clone 268770 3'. 523 e-146  
AA947355, AA947355 od86e12.s1 NCI\_CGAP\_Ov2 Homo sapiens cDNA ... 504 e-140  
AA121074, AA121074 zl88b06.s1 Stratagene colon (#937204) Homo... 460 e-127  
AA742964, AA742964 ny15d01.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 454 e-126  
AA306814, AA306814 EST177885 Colon carcinoma (HCC) cell line ... 452 e-125  
W87699, W87699 zh65b11.r1 Soares fetal liver spleen 1NFLS S1 ... 446 e-123  
W87700, W87700 zh65b11.s1 Soares fetal liver spleen 1NFLS S1 ... 438 e-121  
AA449084, AA449084 zx06b11.s1 Soares total fetus Nb2HF8 9w Ho... 398 e-109  
N99231, N99231 zb76f11.s1 Soares senescent fibroblasts NbHSF ... 391 e-106  
N49900, N49900 yv24d04.s1 Homo sapiens cDNA clone 243655 3'. 383 e-104  
AA782911, AA782911 ai62a10.s1 Soares testis NHT Homo sapiens ... 365 6e-99  
AA936553, AA936553 on23g11.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 361 9e-98  
N74414, N74414 za53c02.s1 Homo sapiens cDNA clone 296258 3'. 353 2e-95  
AA834628, AA834628 od98a10.s1 NCI\_CGAP\_Ov2 Homo sapiens cDNA ... 341 8e-92  
AA693756, AA693756 zi55f11.s1 Soares fetal liver spleen 1NFLS... 341 8e-92  
AA909616, AA909616 ol09d06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 341 8e-92  
H69662, H69662 yr92b03.s1 Homo sapiens cDNA clone 212717 3'. 321 8e-86  
AA249558, AA249558 jj7521.seq.F Human fetal heart, Lambda ZAP... 317 1e-84  
AA911960, AA911960 oh88g08.s1 NCI\_CGAP\_Co8 Homo sapiens cDNA ... 317 1e-84  
AA969099, AA969099 op55e06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 303 2e-80  
AA766191, AA766191 oal2g08.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 212 5e-53  
AA689312, AA689312 nx05e10.s1 NCI\_CGAP\_GC3 Homo sapiens cDNA ... 200 2e-49

AA418586, AA418586 zv93e05.r1 Soares NhHMPu S1 Homo sapiens c... 182 5e-44  
 AA418570, AA418570 zv93e05.s1 Soares NhHMPu S1 Homo sapiens c... 182 5e-44  
 AA534939, AA534939 nf82f03.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 167 3e-39  
 AA888430, AA888430 nw74e05.s1 NCI\_CGAP\_Pr12 Homo sapiens cDNA... 167 3e-39  
 N50003, N50003 yv24d04.r1 Homo sapiens cDNA clone 243655 5' s... 149 6e-34  
 AA535102, AA535102 nf84f06.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 135 1e-29  
 AA262335, AA262335 zr71g03.s1 Soares NhHMPu S1 Homo sapiens c... 129 6e-28  
 AA766681, AA766681 oa34c05.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 105 9e-21  
 AA761492, AA761492 nz27a05.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 101 1e-19  
 AA688350, AA688350 nv15a05.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 90 5e-16  
 AA347041, AA347041 EST53285 Fetal heart II Homo sapiens cDNA ... 76 8e-12  
 T94395, T94395 ye35e02.s1 Homo sapiens cDNA clone 119738 3'. 46 0.007  
 AA833565, AA833565 aj46a02.s1 Soares testis NHT Homo sapiens ... 46 0.007  
 AA095460, AA095460 l4630.seq.F Fetal heart, Lambda ZAP Expres... 40 0.43  
 AA904415, AA904415 ok07e06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 40 0.43  
 AI018800, AI018800 ov32h04.x1 Soares\_testis\_NHT Homo sapiens ... 38 1.7  
 AA631083, AA631083 nq77e07.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 1.7

AA399772, AA399772 vd70g05.r1 Beddington mouse embryonic regi... 347 5e-94  
 AA467106, AA467106 vd98b04.r1 Soares mouse NbMH Mus musculus ... 309 1e-82  
 AI046844, AI046844 uh55c11.r1 Soares mouse embryonic stem cel... 208 3e-52  
 AA475075, AA475075 vh11g05.r1 Soares mouse mammary gland NbMM... 194 4e-48  
 AA646094, AA646094 vs31e06.r1 Stratagene mouse Tcell 937311 M... 186 1e-45  
 AA390020, AA390020 vb30e07.r1 Soares mouse lymph node NbMLN M... 170 6e-41  
 AA245553, AA245553 my52g04.r1 Barstead mouse pooled organs MP... 170 6e-41  
 AA930741, AA930741 vs57b02.r1 Stratagene mouse skin (#937313)... 155 4e-36  
 W62610, W62610 md58c06.r1 Soares mouse embryo NbME13.5 14.5 M... 117 8e-25  
 AA239270, AA239270 my40e01.r1 Barstead mouse pooled organs MP... 109 2e-22  
 AA015148, AA015148 mh16e01.r1 Soares mouse placenta 4NbMP13.5... 54 1e-05  
 AA764095, AA764095 vw09h02.r1 Soares 2NbMT Mus musculus cDNA ... 38 0.61  
 AA238570, AA238570 my35h02.r1 Barstead mouse pooled organs MP... 38 0.61  
 AA600576, AA600576 vm75f08.r1 Knowles Solter mouse blastocyst... 38 0.61  
 AA636273, AA636273 vq76a10.s1 Knowles Solter mouse 2 cell Mus... 36 2.4  
 AA051407, AA051407 mj41f08.r1 Soares mouse embryo NbME13.5 14... 36 2.4  
 AA823136, AA823136 vw41b03.r1 Soares mouse mammary gland NbMM... 36 2.4  
 W83831, W83831 mf26a06.r1 Soares mouse embryo NbME13.5 14.5 M... 36 2.4  
 D77944, MUSC0D06 Mouse embryonal carcinoma F9 cell cDNA, C0D06 36 2.4  
 AA915408, AA915408 vz29h04.r1 Soares 2NbMT Mus musculus cDNA ... 36 2.4  
 AI047229, AI047229 uh63a09.r1 Soares mouse embryonic stem cel... 36 2.4  
 AA271880, AA271880 va73d01.r1 Soares mouse 3NME12 5 Mus muscu... 36 2.4  
 AA475165, AA475165 vg95f01.r1 Barstead mouse pooled organs MP... 36 2.4  
 AA619774, AA619774 vl58a05.s1 Knowles Solter mouse 2 cell Mus... 36 2.4

AA673116, AA673116 vn49g11.r1 Barstead mouse myotubes MPLRB5 ... 36 2.4  
 AA870623, AA870623 vq24a07.r1 Barstead stromal cell line MPLR... 36 2.4  
 W58907, W58907 md52f12.r1 Soares mouse embryo NbME13.5 14.5 M... 36 2.4  
 AA690593, AA690593 vu53d05.r1 Soares mouse mammary gland NbMM... 36 2.4  
 AA754801, AA754801 vu21f03.r1 Barstead mouse myotubes MPLRB5 ... 36 2.4  
 AA271607, AA271607 va72a12.r1 Soares mouse 3NME12 5 Mus muscu... 36 2.4  
 AA064256, AA064256 mj66a03.r1 Soares mouse p3NMF19.5 Mus musc... 36 2.4  
 AA475144, AA475144 vg95d01.r1 Barstead mouse pooled organs MP... 36 2.4  
 AA197736, AA197736 mv02g08.r1 GuayWoodford Beier mouse kidney... 36 2.4

AA817944, AA817944 UI-R-A0-ag-e-01-0-UI.s1 UI-R-A0 Rattus nor... 40 0.14  
 F14714, SSC8B01 S.scrofa mRNA; expressed sequence tag (5'; c... 38 0.54  
 H91505, H91505 SWMFCA089SK Brugia malayi microfilaria cDNA (S... 36 2.1  
 AA998610, AA998610 UI-R-C0-if-c-04-0-UI.s1 UI-R-C0 Rattus nor... 36 2.1  
 AA893562, AA893562 EST197365 Normalized rat liver, Bento Soar... 36 2.1  
 AI008397, AI008397 EST202848 Normalized rat embryo, Bento Soa... 36 2.1

SEQ ID NO:554

Z92544, HS313D11 Human DNA sequence from cosmid 313D11 from ... 700 0.0  
 Z46940, HSPRMTNP2 H.sapiens PRM1 gene, PRM2 gene and TNP2 gene 44 0.048  
 U85039, TMU85039 Theileria mutans 32 kDa immunodominant pirop... 42 0.19  
 U85251, TMU85251 Theileria mutans 32 kDa immunodominant pirop... 42 0.19  
 AF003630, AF003630 Theileria mutans clone 15, 32 kDa immunodo... 42 0.19  
 AF003629, AF003629 Theileria mutans clone 9, 32 kDa immunodom... 42 0.19  
 AB007884, AB007884 Homo sapiens KIAA0424 mRNA, partial cds 42 0.19  
 U85040, TMU85040 Theileria mutans 32 kDa immunodominant pirop... 42 0.19  
 Z97343, ATFCA8 Arabidopsis thaliana DNA chromosome 4, ESSA I... 40 0.75  
 L19655, TOSRNA1X Tomato ringspot virus polyprotein (RNA-1) ge... 40 0.75  
 M73822, TOSRNA1A Tomato ringspot virus RNA1 gene, 5' end. 40 0.75  
 L02543, BOVMTNNT Bos taurus nicotinamide nucleotide transhydr... 40 0.75  
 J03534, BOVNAD Bovine mitochondrial nicotinamide nucleotide t... 40 0.75  
 M62862, TRBRTE Trypanosoma cruzi retrotransposon encoding gag... 40 0.75  
 X72711, MMREPCFC M.musculus mRNA for replication factor C, l... 38 3.0  
 M88489, MUSNBP Mus musculus nonamer binding protein mRNA, com... 38 3.0  
 U36441, MMU36441 Mus musculus differentiation specific elemen... 38 3.0  
 AB002354, AB002354 Human mRNA for KIAA0356 gene, complete cds 38 3.0  
 J03149, CATFMSC Cat (F.domesticus) c-fms proto-oncogene mRNA ... 38 3.0  
 J05475, CHKVICOLL Chicken type VI collagen alpha 2 (VI) subun... 38 3.0



AF038163, AF038163 Homo sapiens interleukin-15 (IL-15) gene, ... 38 3.0  
 X75917, HSFMBMF H.sapiens mRNA for fetal beta-MHC binding fa... 38 3.0  
 X06542, DMHSPG3 Drosophila heat shock gene 3 from 67B locus 38 3.0  
 D17315, DRODAGK Fruit fly mRNA for diacylglycerol kinase, co... 38 3.0  
 Z58600, HS45E3F H.sapiens CpG DNA, clone 45e3, forward read ... 38 3.0  
 D78638, D78638 Xenopus laevis mRNA for DNA (cytosine-5-)-met... 38 3.0  
 Z49204, MMNADPTRH M.musculus mRNA for NADP transhydrogenase. 38 3.0  
 L10425, BPEMETC Bordetella avium beta-cystathionase-lyase (me... 38 3.0  
 U01222, U01222 Mus musculus activator 1 large subunit (A1-p14... 38 3.0  
 U15037, MMU15037 Mus musculus replication factor C large subu... 38 3.0  
 K01643, FCSSMONC Feline sarcoma virus (McDonough strain) tran... 38 3.0  
 Z57538, HS183C6F H.sapiens CpG DNA, clone 183c6, forward rea... 38 3.0  
 U07157, MMU07157 Mus musculus ISRE-binding protein (IBF-1) mR... 38 3.0  
 Z64961, HS183F7R H.sapiens CpG DNA, clone 183f7, reverse rea... 38 3.0

#### HUMAN ESTs

#### SEQ ID NO:555

AF039693, AF039693 Homo sapiens unknown protein mRNA, complet... 916 0.0  
 S51239, S51239 calreticulin [Aplysia californica=marine snail... 48 0.005  
 Z74035, CEF47G9 Caenorhabditis elegans cosmid F47G9, complet... 46 0.019  
 AF022814, AF022814 Fugu rubripes transcription factor (SLP-1)... 44 0.073  
 X82638, CSCYTOX C.sordelii cytotoxin gene 42 0.29  
 U63063, SCU63063 Saccharomyces cerevisiae something about sil... 42 0.29  
 X63501, SCRPC53 S.cerevisiae RPC53 gene for RNA polymerase C... 42 0.29  
 U67572, U67572 Methanococcus jannaschii section 114 of 150 of... 42 0.29  
 Z74201, SCYDL153C S.cerevisiae chromosome IV reading frame O... 42 0.29  
 U66032, MTU66032 Methanosarcina thermophila CO dehydrogenase/... 42 0.29  
 Z95620, SPBC3D6 S.pombe chromosome II cosmid c3D6 42 0.29  
 X97751, SCIV23 S.cerevisiae chrIV genes STE7, CLB3, MSH5, RP... 42 0.29  
 X65541, ATCAN A.thaliana mRNA for carbonic anhydrase 42 0.29  
 L14750, ATHCARANHY Arabidopsis thaliana carbonic anhydrase ge... 42 0.29  
 U00995, U00995 Rattus norvegicus TA1 mRNA, complete cds. 40 1.1  
 S73876, S73876 FPR3=FKBP-70 [Saccharomyces cerevisiae, Genomi... 40 1.1  
 U12825, SCU12825 Saccharomyces cerevisiae transcription facto... 40 1.1  
 Z74237, SCYDL189W S.cerevisiae chromosome IV reading frame O... 40 1.1  
 U76906, REU76906 Rhizobium etli FixK (fixK), FixN (fixN), mon... 40 1.1

AF050157, MMHC135G15 *Mus musculus* major histocompatibility lo... 40 1.1  
 X58857, SCPPH22 *S.cerevisiae* PPH22 gene for protein phosphat... 40 1.1  
 X79379, SCPROIS *S.cerevisiae* gene for proline isomerase 40 1.1  
 Z68341, CEF01G4 *Caenorhabditis elegans* cosmid F01G4, complet... 40 1.1  
 M17192, MUSHOX1 Mouse homeodomain protein (Hox1.1) mRNA, comp... 40 1.1  
 U50307, CELF43H9 *Caenorhabditis elegans* cosmid F43H9. 40 1.1  
 S73144, S73144 bone sialoprotein [cattle, fetal bone cells, m... 40 1.1  
 L34569, YSCFPR3A *Saccharomyces cerevisiae* (clone pBYNG1) prol... 40 1.1  
 D78303, D78303 *Rattus norvegicus* YT521 mRNA for RNA splicing... 40 1.1  
 X83276, SCDNAIV *S.cerevisiae* DNA for ORFs from chromosome IV 40 1.1  
 U54558, HSU54558 Human translation initiation factor eIF3 p66... 40 1.1  
 Z50109, CEC09H10 *Caenorhabditis elegans* cosmid C09H10, compl... 40 1.1  
 X56983, EAVATP1 *E.arvense* gene for catalytic 70kDa V-ATPase ... 40 1.1  
 AB011125, AB011125 *Homo sapiens* mRNA for KIAA0553 protein, p... 40 1.1  
 Z46373, SC8248 *S.cerevisiae* chromosome XIII cosmid 8248 40 1.1  
 AF039042, CELZK697 *Caenorhabditis elegans* cosmid ZK697 40 1.1  
 Z28028, SCYKL028W *S.cerevisiae* chromosome XI reading frame O... 40 1.1  
 AC005266, AC005266 *Homo sapiens* chromosome 19, cosmid F23465,... 38 4.5  
 U60822, HSU60822 Human dystrophin (DMD) gene, exons 7, 8 and ... 38 4.5  
 AJ003141, HVAJ3141 *Hordeum vulgare* mRNA for stress-related p... 38 4.5  
 M26250, CRAGAP43 Goldfish (*C.auratus*) growth-associated prote... 38 4.5  
 X95267, GGRYR3 *G.gallus* mRNA for ryanodine receptor type 3 38 4.5  
 L37092, MUSCDPK *Mus musculus* cyclin-dependent kinase homologu... 38 4.5  
 Z72507, CEF17C11 *Caenorhabditis elegans* cosmid F17C11, compl... 38 4.5  
 U29608, DMU29608 *Drosophila melanogaster* large tumor suppress... 38 4.5  
 Z49072, CET24A11 *Caenorhabditis elegans* cosmid T24A11, compl... 38 4.5  
 M83142, RATBGASTR *Rattus norvegicus* beta-galactoside-alpha 2,... 38 4.5  
 Z20656, HSCAMHCA *Homo sapiens* of cardiac alpha-myosin heavy ... 38 4.5  
 M82937, YSACS2A *Candida albicans* chitin synthase 2 (CHS2) gen... 38 4.5  
 U28888, MMU28888 *Mus musculus* neurogenic differentiation fact... 38 4.5  
 S66408, S66408 c-erbB=proto-oncogene {exon 1, promoter} [chic... 38 4.5  
 AC002396, AC002396 *Arabidopsis thaliana* chromosome I BAC F3I6... 38 4.5  
 AE000665, MMAE000665 *Mus musculus* TCR beta locus from bases 5... 38 4.5  
 L39837, DROWARTS *Drosophila melanogaster* tumor supressor (war... 38 4.5  
 AG000377, AG000377 *Homo sapiens* genomic DNA, 21q region, clo... 38 4.5  
 X05632, HSMHCAG1 Human alpha-MHC gene for myosin heavy chain... 38 4.5  
 AC002108, AC002108 Genomic sequence from Mouse 4, complete se... 38 4.5  
 U37219, HSU37219 Human cyclophilin-like protein CyP-60 mRNA, ... 38 4.5  
 M58633, MUSP58GTA Mouse p58/GTA protein kinase mRNA, complete... 38 4.5  
 M25162, HUMMYHC08 Human cardiac alpha-myosin heavy chain (MYH... 38 4.5  
 Z46259, SCRPD3COS *S.cerevisiae* FY1676 RPD3 gene. 38 4.5  
 U09558, LJU09558 *Lactobacillus johnsonii* ATCC 11506 insertion... 38 4.5  
 U66160, MMUSC104 *Mus musculus* extracellular matrix associated... 38 4.5  
 Z73126, SCYLL021W *S.cerevisiae* chromosome XII reading frame ... 38 4.5  
 U83981, HSU83981 *Homo sapiens* apoptosis associated protein (G... 38 4.5

U59897, MRU59897 *Macropus robustus* hypoxanthine phosphoribosy... 38 4.5  
 D38256, YSCSCT1 Yeast gene for suppressor of ctr mutation 38 4.5  
 X69838, HSG9A *H.sapiens* mRNA for G9a 38 4.5  
 X52952, RNCMOSO Rat mRNA for c-mos 38 4.5  
 U37221, HSU37221 Human cyclophilin-like protein mRNA, partial... 38 4.5  
 X65880, DPRH4OP1 *D.pseudoobscura* rh4 opsin gene, exon 1 38 4.5  
 U58971, NTU58971 *Nicotiana tabacum* calmodulin-binding protein... 38 4.5  
 Z35773, SCYBL012C *S.cerevisiae* chromosome II reading frame O... 38 4.5  
 X67668, MMHMG2 *M.musculus* mRNA for high mobility group 2 pro... 38 4.5  
 L81727, HSL81727 *Homo sapiens* (subclone 1\_d5 from P1 H69) DNA... 38 4.5  
 AL023800, HS833B2 Human DNA sequence \*\*\* SEQUENCING IN PROGR... 38 4.5  
 X62438, HVPERO *H.vulgare* mRNA for peroxidase 38 4.5  
 AC004096, AC004096 Mouse Cosmid ma66a100 from 14D1-D2, comple... 38 4.5  
 AL008980, PFSC03050 *Plasmodium falciparum* DNA \*\*\* SEQUENCING... 38 4.5  
 U64827, MMU64827 *Mus musculus* extracellular matrix associated... 38 4.5  
 AC003010, HUAC003010 *Homo sapiens* Chromosome 16 BAC clone CIT... 38 4.5  
 AE001002, AE001002 *Archaeoglobus fulgidus* section 105 of 172 ... 38 4.5  
 U86662, LEU86662 *Lycopersicon esculentum* VPS41 (tVPS41) mRNA,... 38 4.5  
 M20386, CHKEGFR Chicken epidermal growth factor receptor (CER... 38 4.5  
 M77637, CHKEGF *Gallus gallus* EGF/TGF-alpha receptor (c-erbB) ... 38 4.5  
 U08185, MMU08185 *Mus musculus* BALB/c zinc-finger protein Blim... 38 4.5  
 AC004231, AC004231 *Homo sapiens* chromosome 17, clone hRPC.111... 38 4.5  
 Z50100, HVC39SAT *H.vulgare* GAA-satellite DNA 38 4.5  
 X53731, SCSPA2G *S. cerevisiae* SPA2 gene 38 4.5  
 U37220, HSU37220 Human cyclophilin-like protein mRNA, partial... 38 4.5  
 X97560, SC32KBF *S.cerevisiae* 32kb DNA fragment of chromosome... 38 4.5  
 AB011479, AB011479 *Arabidopsis thaliana* genomic DNA, chromos... 38 4.5  
 U89340, LVU89340 *Lytechinus variegatus* Endo16 homolog (LvEndo1... 38 4.5  
 U73850, TCU73850 *Trypanosoma cruzi* 29 kDa proteasome subunit ... 38 4.5  
 AB006698, AB006698 *Arabidopsis thaliana* genomic DNA, chromos... 38 4.5  
 D37888, CYIMYC2 *Cyprinus carpio* c-myc gene for c-Myc, comple... 38 4.5  
 AF017349, MMDSGIII 7 *Mus musculus* desmoglein 3 (Dsg3) gene, i... 38 4.5  
 X91807, OSTA136 *O.sativa* mRNA for alpha-tubulin (clone OSTA-... 38 4.5  
 Z71587, SCYNL311C *S.cerevisiae* chromosome XIV reading frame ... 38 4.5  
 AE000742, AE000742 *Aquifex aeolicus* section 74 of 109 of the ... 38 4.5

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AA324311, AA324311 EST27136 Cerebellum II *Homo sapiens* cDNA 5... 593 e-167  
 AA639190, AA639190 ns04a01.r1 NCI\_CGAP\_Ew1 *Homo sapiens* cDNA ... 513 e-143  
 AA172199, AA172199 zo96a06.r1 Stratagene ovarian cancer (#937... 505 e-141  
 AA588066, AA588066 nk10d08.s1 NCI\_CGAP\_Co2 *Homo sapiens* cDNA ... 502 e-140  
 AA412036, AA412036 zt68d09.s1 Soares testis NHT *Homo sapiens* ... 502 e-140  
 AA508745, AA508745 ni23a03.s1 NCI\_CGAP\_Co4 *Homo sapiens* cDNA ... 502 e-140

AA480337, AA480337 ne33a03.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 502 e-140  
 AA902270, AA902270 ok69e04.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 502 e-140  
 AA947303, AA947303 ok20d04.s1 Soares\_NSF\_F8\_9W\_OT\_PA\_P\_S1 Hom... 502 e-140  
 R23642, R23642 yh35e03.r1 Homo sapiens cDNA clone 131740 5'. 490 e-136  
 AA811913, AA811913 ob51d06.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 464 e-128  
 AA172083, AA172083 zo96a06.s1 Stratagene ovarian cancer (#937... 464 e-128  
 AA725458, AA725458 ai16g01.s1 Soares parathyroid tumor NbHPA ... 400 e-109  
 R26558, R26558 yh35e02.s1 Homo sapiens cDNA clone 131738 3'. 359 5e-97  
 AA402403, AA402403 zt68d09.r1 Soares testis NHT Homo sapiens ... 315 6e-84  
 R58372, R58372 G3243 Fetal heart Homo sapiens cDNA clone G324... 262 8e-68  
 AA389703, AA389703 M421 Fetal heart, Lambda ZAP Express Homo ... 202 6e-50  
 W25749, W25749 11b4 Human retina cDNA randomly primed sublibr... 103 4e-20  
 W27158, W27158 22h9 Human retina cDNA randomly primed sublibr... 66 1e-08  
 T65784, T65784 yc11f10.s1 Homo sapiens cDNA clone 80395 3' si... 42 0.14  
 AA179601, AA179601 zp49f10.r1 Stratagene HeLa cell s3 937216 ... 42 0.14  
 AA928679, AA928679 on48e08.s1 NCI\_CGAP\_Co8 Homo sapiens cDNA ... 40 0.55  
 AA887972, AA887972 nq95g11.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 40 0.55  
 W46946, W46946 zc40c05.s1 Soares senescent fibroblasts NbHSF ... 40 0.55  
 AA887862, AA887862 nq99b08.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 40 0.55  
 AA554819, AA554819 ni34d08.s1 NCI\_CGAP\_Lu1 Homo sapiens cDNA ... 40 0.55  
 AA557362, AA557362 nl81d12.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 40 0.55  
 AA252258, AA252258 zr29e04.s1 Stratagene NT2 neuronal precurs... 40 0.55  
 N34310, N34310 yy52b10.s1 Homo sapiens cDNA clone 277147 3' s... 40 0.55  
 AA552228, AA552228 nk06b04.s1 NCI\_CGAP\_Co2 Homo sapiens cDNA ... 40 0.55  
 AI017648, AI017648 ou99b02.x1 NCI\_CGAP\_Kid3 Homo sapiens cDNA... 40 0.55  
 T17395, T17395 NIB846 Normalized infant brain, Bento Soares H... 40 0.55  
 AA219659, AA219659 zr05e10.s1 Stratagene NT2 neuronal precurs... 40 0.55  
 AA463841, AA463841 zx67f06.r1 Soares total fetus Nb2HF8 9w Ho... 40 0.55  
 N66817, N66817 za09b11.s1 Homo sapiens cDNA clone 292029 3' s... 40 0.55  
 AA167358, AA167358 zp06f12.s1 Stratagene ovarian cancer (#937... 40 0.55  
 AA063505, AA063505 zf70d02.r1 Soares pineal gland N3HPG Homo ... 40 0.55  
 AA731625, AA731625 nw64a04.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.55  
 AA100119, AA100119 zl80g04.s1 Stratagene colon (#937204) Homo... 40 0.55  
 AA181572, AA181572 zp51d04.s1 Stratagene HeLa cell s3 937216 ... 40 0.55  
 AA327182, AA327182 EST30459 Colon I Homo sapiens cDNA 5' end ... 40 0.55  
 R48608, R48608 yj65f07.s1 Homo sapiens cDNA clone 153637 3' s... 40 0.55  
 AA678485, AA678485 ah06e04.s1 Gessler Wilms tumor Homo sapien... 40 0.55  
 AA082353, AA082353 zn38c11.r1 Stratagene endothelial cell 937... 40 0.55  
 AA633213, AA633213 nq57c06.s1 NCI\_CGAP\_Co9 Homo sapiens cDNA ... 40 0.55  
 W38410, W38410 zc77g09.s1 Pancreatic Islet Homo sapiens cDNA ... 40 0.55  
 AA345893, AA345893 EST51967 Gall bladder I Homo sapiens cDNA ... 40 0.55  
 N26876, N26876 yx97f06.s1 Homo sapiens cDNA clone 269699 3' s... 40 0.55  
 N95279, N95279 zb60c09.s1 Soares fetal lung NbHL19W Homo sapi... 40 0.55  
 AI041637, AI041637 ox92h08.x1 Soares\_senescent\_fibroblasts\_Nb... 40 0.55  
 N67830, N67830 za05d12.s1 Homo sapiens cDNA clone 291671 3' s... 40 0.55

AA535094, AA535094 nf84e06.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.55  
AA514414, AA514414 nf57d11.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.55  
T56802, T56802 ya71h07.s2 Homo sapiens cDNA clone 67165 3' co... 40 0.55  
N68147, N68147 yz55f12.s1 Homo sapiens cDNA clone 286991 3' s... 40 0.55  
AA535811, AA535811 nf93g10.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.55  
AA115591, AA115591 zl05g09.s1 Soares pregnant uterus NbHPU Ho... 40 0.55  
N75851, N75851 za96g11.s1 Homo sapiens cDNA clone 300452 3'. 40 0.55  
AA534433, AA534433 nf80a08.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.55  
H99778, H99778 yx36g01.s1 Homo sapiens cDNA clone 263856 3' s... 40 0.55  
AA970859, AA970859 oo81h03.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.55  
F02131, HSC0PF092 H. sapiens partial cDNA sequence; clone c-... 40 0.55  
AA810279, AA810279 od14g11.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.55  
AA595146, AA595146 nl84b01.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 40 0.55  
AA632386, AA632386 np67e06.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 40 0.55  
AA135124, AA135124 zo24c04.s1 Stratagene colon (#937204) Homo... 40 0.55  
AA143500, AA143500 zo31b10.s1 Stratagene colon (#937204) Homo... 40 0.55  
AA854992, AA854992 aj53g12.s1 Soares testis NHT Homo sapiens ... 40 0.55  
AA156872, AA156872 zl20h07.s1 Soares pregnant uterus NbHPU Ho... 40 0.55  
AA160994, AA160994 zq41c12.s1 Stratagene hNT neuron (#937233)... 40 0.55  
AA961724, AA961724 or60a10.s1 NCI\_CGAP\_GC3 Homo sapiens cDNA ... 40 0.55  
AA551210, AA551210 nj27e09.s1 NCI\_CGAP\_AA1 Homo sapiens cDNA ... 40 0.55  
R44103, R44103 yg27c10.s1 Homo sapiens cDNA clone 33636 3'. 40 0.55  
AA938086, AA938086 oj08h08.s1 NCI\_CGAP\_Mel3 Homo sapiens cDNA... 40 0.55  
AA576021, AA576021 nm57d11.s1 NCI\_CGAP\_Br3 Homo sapiens cDNA ... 40 0.55  
AA722725, AA722725 zg86b09.s1 Soares fetal heart NbHH19W Homo... 40 0.55  
AA678948, AA678948 ah08h11.s1 Gessler Wilms tumor Homo sapien... 40 0.55  
W07435, W07435 za96g11.r1 Soares fetal lung NbHL19W Homo sapi... 40 0.55  
T34639, T34639 EST72167 Homo sapiens cDNA 5' end similar to s... 40 0.55  
AA632245, AA632245 np67b09.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 40 0.55  
R98701, R98701 yr31f08.s1 Homo sapiens cDNA clone 206919 3'. 40 0.55  
R76418, R76418 yi58a10.s1 Homo sapiens cDNA clone 143418 3'. 40 0.55  
AI028447, AI028447 ow08b09.x1 Soares parathyroid tumor NbHPA ... 40 0.55  
AI002929, AI002929 an15e12.s1 Gessler Wilms tumor Homo sapien... 40 0.55  
AA779388, AA779388 ae26a03.s1 Soares NbHFB Homo sapiens cDNA ... 40 0.55  
AA776220, AA776220 ah10f02.s1 Gessler Wilms tumor Homo sapien... 40 0.55  
AA815223, AA815223 oc05c04.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.55  
W60807, W60807 zd27b08.s1 Soares fetal heart NbHH19W Homo sap... 40 0.55  
AA666007, AA666007 ag71g01.s1 Gessler Wilms tumor Homo sapien... 40 0.55  
AA643849, AA643849 np26f07.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 40 0.55  
AA846740, AA846740 aj99b12.s1 Soares parathyroid tumor NbHPA ... 40 0.55  
AA598498, AA598498 ae38h01.s1 Gessler Wilms tumor Homo sapien... 40 0.55  
AA535972, AA535972 nf95a01.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.55  
AA488544, AA488544 ab37g06.r1 Stratagene HeLa cell s3 937216 ... 40 0.55  
AA866044, AA866044 oh52g07.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 40 0.55  
C14370, C14370 Human fetal brain cDNA 5'-end GEN-050F01 40 0.55

AA237204, AA237204 mx18d02.r1 Soares mouse NML Mus musculus c... 167 1e-39  
 AA563402, AA563402 vl75d08.r1 Knowles Solter mouse blastocyst... 38 0.78  
 AA413261, AA413261 ve52f04.r1 Beddington mouse embryonic regi... 38 0.78  
 AA097645, AA097645 mm36f09.r1 Stratagene mouse skin (#937313)... 38 0.78  
 AA122578, AA122578 mn25b08.r1 Beddington mouse embryonic regi... 38 0.78  
 AA122581, AA122581 mn25c08.r1 Beddington mouse embryonic regi... 38 0.78  
 AA646168, AA646168 vn11e06.r1 Stratagene mouse Tcell 937311 M... 36 3.1  
 AA200881, AA200881 mu03c09.r1 Soares mouse 3NbMS Mus musculus... 36 3.1  
 AI048938, AI048938 uc84h06.y1 Sugano mouse kidney mkia Mus mu... 36 3.1  
 AA217675, AA217675 mv01b09.r1 Soares mouse lymph node NbMLN M... 36 3.1  
 AI006387, AI006387 ua71d09.r1 Soares 2NbMT Mus musculus cDNA ... 36 3.1  
 AA162722, AA162722 mn42b07.r1 Beddington mouse embryonic regi... 36 3.1  
 AA207387, AA207387 mv89a11.r1 GuayWoodford Beier mouse kidney... 36 3.1  
 AA511382, AA511382 vg14b04.r1 Soares mouse NbMH Mus musculus ... 36 3.1  
 AA123112, AA123112 mn30g01.r1 Beddington mouse embryonic regi... 36 3.1  
 AA106683, AA106683 ml83h06.r1 Stratagene mouse kidney (#93731... 36 3.1  
 AA105882, AA105882 ml84h07.r1 Stratagene mouse kidney (#93731... 36 3.1  
 W12171, W12171 ma59a10.r1 Soares mouse p3NMF19.5 Mus musculus... 36 3.1  
 AA208446, AA208446 mv85e01.r1 GuayWoodford Beier mouse kidney... 36 3.1  
 AA451370, AA451370 vf84h02.r1 Soares mouse mammary gland NbMM... 36 3.1  
 AA244639, AA244639 mx02g12.r1 Soares mouse NML Mus musculus c... 36 3.1  
 AA267119, AA267119 mz74d07.r1 Soares mouse lymph node NbMLN M... 36 3.1  
 AA561847, AA561847 vl27a12.r1 Stratagene mouse Tcell 937311 M... 36 3.1  
 AA237313, AA237313 mx17b11.r1 Soares mouse NML Mus musculus c... 36 3.1  
 AA145817, AA145817 mq68a12.r1 Soares 2NbMT Mus musculus cDNA ... 36 3.1  
 AA052080, AA052080 mf69f12.r1 Soares mouse embryo NbME13.5 14... 36 3.1  
 AA000646, AA000646 mg23f09.r1 Soares mouse embryo NbME13.5 14... 36 3.1  
 AA510521, AA510521 vh59a05.r1 Soares mouse mammary gland NbMM... 36 3.1  
 AI006122, AI006122 ua86h01.r1 Soares mouse mammary gland NbMM... 36 3.1  
 AA987039, AA987039 uc74e05.x1 Sugano mouse liver mlia Mus mus... 36 3.1  
 W77413, W77413 me64d06.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.1  
 AA114809, AA114809 mn17e09.r1 Beddington mouse embryonic regi... 36 3.1  
 AA793564, AA793564 vn54c05.r1 Barstead mouse myotubes MPLRB5 ... 36 3.1  
 AA174537, AA174537 mt10f09.r1 Soares mouse 3NbMS Mus musculus... 36 3.1  
 W62181, W62181 md87d08.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.1  
 AA272905, AA272905 va39d01.r1 Soares mouse 3NME12 5 Mus muscu... 36 3.1  
 AA286005, AA286005 va30e05.r1 GuayWoodford Beier mouse kidney... 36 3.1  
 AA212823, AA212823 mw81c07.r1 Soares mouse NML Mus musculus c... 36 3.1  
 AA125061, AA125061 mq83d10.r1 Stratagene mouse melanoma (#937... 36 3.1

AA519228, AA519228 TgESTzz39h02.s1 TgME49 invivo Bradyzoite c... 44 0.011

AA520185, AA520185	TgESTzz39d03.s1	TgME49 invivo	Bradyzoite c...	44	0.011
AA531917, AA531917	TgESTzz48f01.r1	TgME49 invivo	Bradyzoite c...	44	0.011
AA519997, AA519997	TgESTzz36h03.r1	TgME49 invivo	Bradyzoite c...	44	0.011
AA520811, AA520811	TgESTzz64d05.r1	TgME49 invivo	Bradyzoite c...	44	0.011
AA520866, AA520866	TgESTzz68e05.r1	TgME49 invivo	Bradyzoite c...	44	0.011
AA519844, AA519844	TgESTzz36c03.r1	TgME49 invivo	Bradyzoite c...	44	0.011
AA274295, AA274295	TgESTzz24c11.s1	TgME49 invivo	Bradyzoite c...	44	0.011
AA520901, AA520901	TgESTzz65a05.r1	TgME49 invivo	Bradyzoite c...	44	0.011
AA519829, AA519829	TgESTzz36a02.r1	TgME49 invivo	Bradyzoite c...	44	0.011
AA531839, AA531839	TgESTzz47h05.r1	TgME49 invivo	Bradyzoite c...	44	0.011
C70525, C70525	C.elegans cDNA clone yk409g6 : 5' end, single...			44	0.011
AA520235, AA520235	TgESTzz53c06.r1	TgME49 invivo	Bradyzoite c...	42	0.044
T42800, T42800	6063 Lambda-PRL2 Arabidopsis thaliana cDNA clo...			42	0.044
R29976, R29976	12581 Lambda-PRL2 Arabidopsis thaliana cDNA cl...			42	0.044
H32045, H32045	EST106774 Rat PC-12 cells, untreated Rattus sp...			40	0.18
AA819924, AA819924	MF5MA171.AE3 S. mansoni female adult Lambd...			40	0.18
H37128, H37128	15257 Lambda-PRL2 Arabidopsis thaliana cDNA cl...			40	0.18
T04367, T04367	414 Lambda-PRL2 Arabidopsis thaliana cDNA clon...			40	0.18
R90528, R90528	16883 Lambda-PRL2 Arabidopsis thaliana cDNA cl...			40	0.18
AA660422, AA660422	00298 MtrHE Medicago truncatula cDNA 5'			40	0.18
U94861, RRU94861	Rattus norvegicus clone HCY3 mRNA sequence			40	0.18
F14275, ATTS5197	A. thaliana transcribed sequence; clone YBY...			38	0.69
W43730, W43730	23107 CD4-16 Arabidopsis thaliana cDNA clone H...			38	0.69
N65025, N65025	20065 Lambda-PRL2 Arabidopsis thaliana cDNA cl...			38	0.69
AI001628, AI001628	EST0210 Tilapia brain cDNA library in pUC1...			38	0.69
H74687, H74687	383 Brassica napus cDNA clone R25R.			38	0.69
AA395597, AA395597	27394 Lambda-PRL2 Arabidopsis thaliana cDN...			38	0.69
AA753070, AA753070	97AS2091 Rice Immature Seed Lambda ZAPII c...			38	0.69
D41274, RICS3647A	Rice cDNA, partial sequence (S3647_1A).			38	0.69
Z25731, ATTS1208	A. thaliana transcribed sequence; clone VCV...			38	0.69
N82780, N82780	TgESTzy34e03.r1 TgRH Tachyzoite cDNA Toxoplasm...			38	0.69
AA597822, AA597822	29889 Lambda-PRL2 Arabidopsis thaliana cDN...			38	0.69
AA948906, AA948906	LD27590.5prime LD Drosophila melanogaster ...			38	0.69
AI013695, AI013695	EST208370 Normalized rat spleen, Bento Soa...			38	0.69
AA753263, AA753263	96BS0294 Rice Immature Seed Lambda ZAPII c...			38	0.69
F14402, ATTS5324	A. thaliana transcribed sequence; clone TAP...			36	2.7
T46158, T46158	9421 Lambda-PRL2 Arabidopsis thaliana cDNA clo...			36	2.7
C91400, C91400	Dictyostelium discoideum slug cDNA, clone SSK169			36	2.7
T46009, T46009	9272 Lambda-PRL2 Arabidopsis thaliana cDNA clo...			36	2.7
AA440655, AA440655	LD15510.5prime LD Drosophila melanogaster ...			36	2.7
AA559374, AA559374	MU002092.NH3 York-Harrop-lung-A Schistosom...			36	2.7
Z32623, ATTS2751	A. thaliana transcribed sequence; clone YAP...			36	2.7
T43683, T43683	6946 Lambda-PRL2 Arabidopsis thaliana cDNA clo...			36	2.7
AA263535, AA263535	LD06645.5prime LD Drosophila melanogaster ...			36	2.7
C37095, C37095	C.elegans cDNA clone yk482c11 : 3' end, singl...			36	2.7

C57017, C57017 *C.elegans* cDNA clone yk308h9 : 3' end, single... 36 2.7  
 C93857, C93857 *Dictyostelium discoideum* slug cDNA, clone SSL794 36 2.7  
 C92242, C92242 *Dictyostelium discoideum* slug cDNA, clone SSD283 36 2.7  
 Z33976, ATTS3037 *A. thaliana* transcribed sequence; clone YAP... 36 2.7  
 R62091, R62091 EST351 *Strongylocentrotus purpuratus* cDNA 5' end. 36 2.7  
 AA567455, AA567455 HL01288.5prime HL *Drosophila melanogaster* ... 36 2.7  
 C74456, C74456 Rice cDNA, partial sequence (E31357\_1A) 36 2.7  
 AA753227, AA753227 97AS2316 Rice Immature Seed Lambda ZAPII c... 36 2.7  
 C92456, C92456 *Dictyostelium discoideum* slug cDNA, clone SSE569 36 2.7  
 T20458, T20458 2466 Lambda-PRL2 *Arabidopsis thaliana* cDNA clo... 36 2.7  
 R29905, R29905 12510 Lambda-PRL2 *Arabidopsis thaliana* cDNA cl... 36 2.7  
 M79841, M79841 wEST00378 *Caenorhabditis elegans* cDNA clone CE... 36 2.7  
 Z17562, ATTS0136 *A. thaliana* transcribed sequence; clone TAT... 36 2.7  
 D71983, CELK084H2R *C.elegans* cDNA clone yk84h2 : 3' end, sin... 36 2.7  
 T20404, T20404 2412 Lambda-PRL2 *Arabidopsis thaliana* cDNA clo... 36 2.7  
 AI012789, AI012789 EST207240 Normalized rat placenta, Bento S... 36 2.7  
 U83048, BTU83048 *Bos taurus* clone 0429 mRNA sequence 36 2.7  
 AA660182, AA660182 00022 MtRHE *Medicago truncatula* cDNA 5' si... 36 2.7  
 D48514, RICS14740A Rice cDNA, partial sequence (S14740\_1A). 36 2.7  
 C90110, C90110 *Dictyostelium discoideum* slug cDNA, clone SSI103 36 2.7  
 H36880, H36880 15009 Lambda-PRL2 *Arabidopsis thaliana* cDNA cl... 36 2.7  
 AA699152, AA699152 HL07807.5prime HL *Drosophila melanogaster* ... 36 2.7  
 C11922, C11922 *C.elegans* cDNA clone yk144a11 : 5' end, singl... 36 2.7  
 AA816691, AA816691 LD03795.5prime LD *Drosophila melanogaster* ... 36 2.7

SEQ ID NO:556

X99668, MM22A3 *M.musculus* mRNA for exon from unknown gene 22A3 260 5e-67  
 Z83760, CICOS41 *Ciona intestinalis* DNA sequence from cosmid ... 40 0.94  
 Z75710, CED1081 *Caenorhabditis elegans* cosmid D1081, complet... 40 0.94  
 U73628, HSU73628 Human chromosome 11 101h11 cosmid, complete ... 40 0.94  
 X99757, DMDYDTRO *D.melanogaster* mRNA for dystrophin 38 3.7  
 U51189, HIVU51189 HIV-1 clone 93th253 from Thailand, complete... 38 3.7  
 AC004118, AC004118 *Drosophila melanogaster* (P1 DS06238 (D26))... 38 3.7  
 U50313, CELF44C4 *Caenorhabditis elegans* cosmid F44C4. 38 3.7  
 AC004503, AC004503 *Homo sapiens* chromosome 5, P1 clone 1354A7... 38 3.7  
 M16840, WHTCPA2 Wheat Asp-tRNA gene. 38 3.7  
 Y13381, RNAMPH1 *Rattus norvegicus* mRNA for amphiphysin, amph1 38 3.7  
 AC002994, AC002994 *Homo sapiens* chromosome 17, clone HRPC987K... 38 3.7  
 AB008271, AB008271 *Arabidopsis thaliana* genomic DNA, chromos... 38 3.7  
 D49701, ASNNIAD *Aspergillus oryzae* niaD gene for nitrate red... 38 3.7



X59422, HSPLD1 H.sapiens Pl d1 repetitive DNA 38 3.7  
 Z98555, PFSC03027 Plasmodium falciparum DNA \*\*\* SEQUENCING I... 38 3.7

# HUMAN ESTs

AA315671, AA315671 EST187451 Colon carcinoma (HCC) cell line ... 932 0.0  
 U56653, HSU56653 Human heat shock inducible mRNA 769 0.0  
 AA487685, AA487685 ab23b09.r1 Stratagene lung (#937210) Homo ... 751 0.0  
 AA044797, AA044797 zk67g12.r1 Soares pregnant uterus NbHPU Ho... 749 0.0  
 AA314922, AA314922 EST186735 HCC cell line (matastasis to liv... 698 0.0  
 AA082278, AA082278 zn42d12.r1 Stratagene endothelial cell 937... 668 0.0  
 H22613, H22613 yn64f03.r1 Homo sapiens cDNA clone 173213 5'. 624 e-177  
 AA044743, AA044743 zk67g12.s1 Soares pregnant uterus NbHPU Ho... 622 e-176  
 AA487470, AA487470 ab23b09.s1 Stratagene lung (#937210) Homo ... 601 e-170  
 AA121057, AA121057 zm22b03.r1 Stratagene pancreas (#937208) H... 581 e-164  
 AA194396, AA194396 zq05g05.s1 Stratagene muscle 937209 Homo s... 535 e-150  
 AA384283, AA384283 EST97787 Thyroid Homo sapiens cDNA 5' end 535 e-150  
 AA669015, AA669015 ab88f01.s1 Stratagene lung (#937210) Homo ... 535 e-150  
 AA194336, AA194336 zq05g05.r1 Stratagene muscle 937209 Homo s... 505 e-141  
 R96173, R96173 yt84e09.r1 Homo sapiens cDNA clone 231016 5'. 486 e-135  
 AA028934, AA028934 zk08b09.s1 Soares pregnant uterus NbHPU Ho... 484 e-134  
 AA564849, AA564849 nj22c04.s1 NCI\_CGAP\_AA1 Homo sapiens cDNA ... 442 e-122  
 AA932576, AA932576 oo57g10.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 440 e-121  
 AA876265, AA876265 oi12g09.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 434 e-120  
 AA025525, AA025525 ze86a11.s1 Soares fetal heart NbHH19W Homo... 430 e-118  
 U56654, HSU56654 Human heat shock inducible mRNA 426 e-117  
 AA746600, AA746600 nx18c02.s1 NCI\_CGAP\_GC3 Homo sapiens cDNA ... 406 e-111  
 AA876346, AA876346 oj24a11.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 406 e-111  
 W23082, W23082 78D1 Human retina cDNA Tsp509I-cleaved sublibr... 402 e-110  
 AI034059, AI034059 owl4h11.x1 Soares parathyroid tumor NbHPA ... 357 2e-96  
 AA662934, AA662934 nu92d09.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 323 2e-86  
 AA844331, AA844331 ai95f01.s1 Soares parathyroid tumor NbHPA ... 301 8e-80  
 AA249866, AA249866 y0761.seq.F Human fetal heart, Lambda ZAP ... 297 1e-78  
 R19215, R19215 yg24b07.r1 Homo sapiens cDNA clone 33126 5'. 280 3e-73  
 T39355, T39355 ya04g08.r1 Homo sapiens cDNA clone 60542 5'. 254 2e-65  
 AA731264, AA731264 nw57c08.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 220 2e-55  
 AA768549, AA768549 oa67c07.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 220 2e-55  
 AA668506, AA668506 ac49a11.s1 Stratagene hNT neuron (#937233)... 216 4e-54  
 T55337, T55337 yb79b05.s1 Homo sapiens cDNA clone 77361 3'. 198 8e-49  
 AA860575, AA860575 aj86a09.s1 Soares parathyroid tumor NbHPA ... 198 8e-49  
 AA335548, AA335548 EST39962 Epididymus Homo sapiens cDNA 5' end 109 6e-22  
 R13183, R13183 yf73f02.r1 Homo sapiens cDNA clone 27960 5'. 58 2e-06  
 T80034, T80034 yd04c06.r1 Homo sapiens cDNA clone 24672 5'. 38 1.8  
 AA595230, AA595230 nl84g02.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 38 1.8

002050-62623460

AA871935, AA871935 vq42h02.r1 Barstead bowel MPLRB9 Mus muscu... 664 0.0  
 AA062330, AA062330 ml35e10.r1 Stratagene mouse testis (#93730... 589 e-167  
 AI048164, AI048164 ud71b09.y1 Sugano mouse liver mlia Mus mus... 537 e-151  
 W08037, W08037 mb37h01.r1 Soares mouse p3NMF19.5 Mus musculus... 462 e-128  
 AA387311, AA387311 vc19a03.r1 Ko mouse embryo 11 5dpc Mus mus... 264 6e-69  
 AA163072, AA163072 ms31a11.r1 Stratagene mouse skin (#937313)... 212 2e-53  
 AA596763, AA596763 vm60a10.r1 Stratagene mouse Tcell 937311 M... 178 3e-43  
 AA562549, AA562549 vl63a11.r1 Knowles Solter mouse blastocyst... 143 2e-32  
 AA212378, AA212378 mu44c03.r1 Soares 2NbMT Mus musculus cDNA ... 113 1e-23  
 AA450862, AA450862 vg55h12.r1 Beddington mouse embryonic regi... 111 5e-23  
 AA990073, AA990073 ua59a01.r1 Soares 2NbMT Mus musculus cDNA ... 86 3e-15  
 AA921175, AA921175 vy54b10.r1 Stratagene mouse lung 937302 Mu... 78 8e-13  
 AA261119, AA261119 mz89e01.r1 Soares mouse NML Mus musculus c... 38 0.65  
 AI005952, AI005952 ua80f06.r1 Soares 2NbMT Mus musculus cDNA ... 36 2.6  
 AA123274, AA123274 mn23a08.r1 Beddington mouse embryonic regi... 36 2.6  
 AI036828, AI036828 vw96c02.r1 Stratagene mouse skin (#937313)... 36 2.6

H35787, H35787 EST109178 Rat PC-12 cells, NGF-treated (9 days... 105 3e-21  
 AA686082, AA686082 EST109179 Rat PC-12 cells, NGF-treated (9 ... 86 3e-15  
 C23464, C23464 Jpanese flounder liver cDNA, LE5(10) 72 4e-11  
 C23465, C23465 Jpanese flounder liver cDNA, LE5(10) 56 2e-06  
 AA520314, AA520314 TgESTzz38h12.r1 TgME49 invivo Bradyzoite c... 38 0.57  
 AA520085, AA520085 TgESTzz37g05.r1 TgME49 invivo Bradyzoite c... 38 0.57  
 AA520033, AA520033 TgESTzz36f10.r1 TgME49 invivo Bradyzoite c... 38 0.57  
 AA012516, AA012516 TgESTzz23f04.r1 TgME49cDNA Toxoplasma gond... 38 0.57  
 AA274286, AA274286 TgESTzz24c01.s1 TgME49 invivo Bradyzoite c... 38 0.57  
 AA660585, AA660585 00471 MtrHE Medicago truncatula cDNA 5' si... 38 0.57  
 L35828, BNAESTBD Brassica rapa (clone F0621) expressed sequen... 38 0.57  
 AA520070, AA520070 TgESTzz37e05.r1 TgME49 invivo Bradyzoite c... 38 0.57  
 C30080, C30080 C.elegans cDNA clone yk236c3 : 3' end, single... 36 2.3  
 C39044, C39044 C.elegans cDNA clone yk505a4 : 3' end, single... 36 2.3  
 C55023, C55023 C.elegans cDNA clone yk422a3 : 3' end, single... 36 2.3  
 AA542589, AA542589 fa08d06.s1 Zebrafish ICRFzfls Danio rerio ... 36 2.3  
 N25370, N25370 EST000480 Schistosoma mansoni cDNA clone SMTBA... 36 2.3  
 AA820625, AA820625 LD24443.5prime LD Drosophila melanogaster ... 36 2.3  
 AA494922, AA494922 fa12g10.r1 Zebrafish ICRFzfls Danio rerio ... 36 2.3  
 AA495181, AA495181 fa04d06.s1 Zebrafish ICRFzfls Danio rerio ... 36 2.3  
 D73287, CELK116G6R C.elegans cDNA clone yk116g6 : 3' end, si... 36 2.3  
 C28238, C28238 Rice cDNA, partial sequence (C60429\_1A) 36 2.3

002090 6663160

SEQ ID NO:557

AF039693, AF039693	Homo sapiens unknown protein mRNA, complet...	948	0.0
S51239, S51239	calreticulin [ <i>Aplysia californica</i> =marine snail...	56	1e-05
Z74035, CEF47G9	<i>Caenorhabditis elegans</i> cosmid F47G9, complet...	46	0.012
U25723, CPU25723	<i>Cavia porcellus</i> alpha-2B adrenoceptor gene, ...	44	0.047
AL021407, HS13D10	Homo sapiens DNA sequence from PAC 13D10 o...	42	0.19
U67572, U67572	<i>Methanococcus jannaschii</i> section 114 of 150 of...	42	0.19
V01470, ZMZE01	<i>Zea mays</i> gene encoding a zein gene (clone lam...	42	0.19
U06631, HSU06631	Human (H326) mRNA, complete cds.	42	0.19
X82638, CSCYTOX	<i>C.sordelii</i> cytotoxin gene	42	0.19
AE000926, AE000926	<i>Methanobacterium thermoautotrophicum</i> from ...	42	0.19
AC004135, AC004135	Genomic sequence for <i>Arabidopsis thaliana</i> ...	42	0.19
AC003010, HUAC003010	Homo sapiens Chromosome 16 BAC clone CIT...	40	0.74
AF050157, MMHC135G15	<i>Mus musculus</i> major histocompatibility lo...	40	0.74
AC002352, AC002352	Homo sapiens 12q24 PAC P256D10 complete se...	40	0.74
X07699, MMNUCLEO	Mouse nucleolin gene	40	0.74
X02399, MMHOM6	Mouse embryonal carcinoma DNA fragment contai...	40	0.74
M93661, RATNOTCHX	Rat notch 2 mRNA.	40	0.74
M17440, MUSMHC4H2S	Mouse MHC (H-2) S region complement compon...	40	0.74
U15972, MMU15972	<i>Mus musculus</i> homeobox ( <i>Hoxa7</i> ) gene, complete...	40	0.74
AB001601, AB001601	Homo sapiens DBP2 mRNA for ATP-dependent ...	40	0.74
U09820, HSU09820	Human helicase II ( <i>RAD54L</i> ) mRNA, complete cds.	40	0.74
AB011149, AB011149	Homo sapiens mRNA for KIAA0577 protein, c...	40	0.74
U26259, MMU26259	<i>Mus musculus</i> C2-H2 zinc finger protein mRNA,...	40	0.74
L48363, MUSZFPTR	<i>Mus musculus</i> zinc finger protein gene, compl...	40	0.74
AC003113, AC003113	<i>Arabidopsis thaliana</i> BAC F24O1 chromosome ...	40	0.74
D76432, D76432	Mouse mRNA for transcriptional repressor delt...	40	0.74
U72937, HSU72937	Human putative DNA dependent ATPase and heli...	40	0.74
U72915, HSATRX16	Human putative DNA dependent ATPase and heli...	40	0.74
U00995, U00995	<i>Rattus norvegicus</i> TA1 mRNA, complete cds.	40	0.74
Z48618, SCCHVII35	<i>S.cerevisiae</i> genes for <i>RAD54</i> , <i>ACE1</i> (CUP2), ...	40	0.74
U75653, HSU75653	Human zinc finger helicase ( <i>Znf-HX</i> ) mRNA, co...	40	0.74
Z72672, SCYGL150C	<i>S.cerevisiae</i> chromosome VII reading frame ...	40	0.74
Z50109, CEC09H10	<i>Caenorhabditis elegans</i> cosmid C09H10, compl...	40	0.74
AF013969, AF013969	<i>Mus musculus</i> antigen containing epitope to...	40	0.74
M95627, HUMAAMP1X	Homo sapiens angio-associated migratory cel...	40	0.74
U72936, HSU72936	Human putative DNA dependent ATPase and heli...	40	0.74
M88753, DROHTCHRP1	Fruitfly heterochromatin protein-1 gene, c...	40	0.74
U76906, REU76906	<i>Rhizobium etli</i> FixK ( <i>fixK</i> ), <i>FixN</i> ( <i>fixN</i> ), mon...	40	0.74
U97085, HSNP14	Homo sapiens X-linked nuclear protein ( <i>ATRX</i> ) ...	40	0.74
L34363, HUMNUCPRO	Human X-linked nuclear protein ( <i>XNP</i> ) gene, ...	40	0.74
U72938, HSU72938	Human putative DNA dependent ATPase and heli...	40	0.74

X56983, EAVATP1 E.arvense gene for catalytic 70kDa V-ATPase ... 40 0.74  
 U88539, MMU88539 Mus musculus chromatin structural protein ho... 40 0.74  
 U07704, HSU07704 Human protein kinase PITSLRE isoform PBETA21... 38 2.9  
 U07705, HSU07705 Human protein kinase PITSLRE isoform PBETA22... 38 2.9  
 AF019612, AF019612 Homo sapiens S2P mRNA, complete cds 38 2.9  
 U04818, HSU04818 Human protein kinase PITSLRE alpha 2-4 mRNA,... 38 2.9  
 AB002381, AB002381 Human mRNA for KIAA0383 gene, partial cds 38 2.9  
 AB009520, AB009520 Pyrococcus horikoshii OT3 genomic DNA, 13... 38 2.9  
 Z83848, HS57A13 Human DNA sequence from PAC 57A13 between ma... 38 2.9  
 AC004592, AC004592 Homo sapiens PAC clone DJ0244J05 from 5q31... 38 2.9  
 L11710, ZEFZCMYC Brachydanio rerio c-myc oncoprotein mRNA, co... 38 2.9  
 D43920, CHKMETASE Chicken mRNA for DNA (cytosine-5-)-methylt... 38 2.9  
 U49056, RNU49056 Rattus norvegicus CTD-binding SR-like protei... 38 2.9  
 U04824, HSU04824 Human protein kinase PITSLRE alpha 2-1 mRNA,... 38 2.9  
 U78045, HSU78045 Human collagenase and stromelysin genes, com... 38 2.9  
 U04816, HSU04816 Human protein kinase PITSLRE alpha 2-2 mRNA,... 38 2.9  
 U04817, HSU04817 Human protein kinase PITSLRE alpha 2-3 mRNA,... 38 2.9

#### HUMAN ESTs

AA639190, AA639190 ns04a01.r1 NCI\_CGAP\_Ew1 Homo sapiens cDNA ... 519 e-145  
 AA172199, AA172199 zo96a06.r1 Stratagene ovarian cancer (#937... 513 e-144  
 R23642, R23642 yh35e03.r1 Homo sapiens cDNA clone 131740 5'. 490 e-136  
 AA902270, AA902270 ok69e04.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 450 e-124  
 AA947303, AA947303 ok20d04.s1 Soares\_NSF\_F8\_9W\_OT\_PA\_P\_S1 Hom... 402 e-110  
 AA588066, AA588066 nk10d08.s1 NCI\_CGAP\_Co2 Homo sapiens cDNA ... 347 1e-93  
 AA412036, AA412036 zt68d09.s1 Soares testis NHT Homo sapiens ... 347 1e-93  
 AA480337, AA480337 ne33a03.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 347 1e-93  
 AA508745, AA508745 ni23a03.s1 NCI\_CGAP\_Co4 Homo sapiens cDNA ... 347 1e-93  
 AA172083, AA172083 zo96a06.s1 Stratagene ovarian cancer (#937... 315 4e-84  
 AA811913, AA811913 ob51d06.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 299 2e-79  
 AA402403, AA402403 zt68d09.r1 Soares testis NHT Homo sapiens ... 299 2e-79  
 AA725458, AA725458 ai16g01.s1 Soares parathyroid tumor NbHPA ... 250 2e-64  
 R26558, R26558 yh35e02.s1 Homo sapiens cDNA clone 131738 3'. 250 2e-64  
 W25749, W25749 11b4 Human retina cDNA randomly primed sublibr... 103 3e-20  
 W27158, W27158 22h9 Human retina cDNA randomly primed sublibr... 66 6e-09  
 AA737681, AA737681 nw63c04.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 42 0.090  
 T65784, T65784 yc11f10.s1 Homo sapiens cDNA clone 80395 3' si... 42 0.090  
 R52021, R52021 yg84h09.r1 Homo sapiens cDNA clone 40181 5' si... 42 0.090  
 AA569993, AA569993 nm47h04.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 42 0.090  
 R50149, R50149 yj61c05.s1 Homo sapiens cDNA clone 153224 3' s... 42 0.090  
 R87930, R87930 yo47a11.s1 Homo sapiens cDNA clone 181052 3' s... 42 0.090  
 AA812204, AA812204 ob84f01.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 42 0.090  
 AA770224, AA770224 ah82e12.s1 Soares testis NHT Homo sapiens ... 42 0.090

D29591, HUMNK752 Human keratinocyte cDNA, clone 752 40 0.36  
 AA324325, AA324325 EST27219 Cerebellum II Homo sapiens cDNA 5... 40 0.36  
 AA053063, AA053063 zl71c03.r1 Stratagene colon (#937204) Homo... 40 0.36  
 T35539, T35539 EST86964 Homo sapiens cDNA 5' end similar to N... 40 0.36  
 AA974278, AA974278 oq14d03.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 40 0.36  
 W26196, W26196 22b5 Human retina cDNA randomly primed sublibr... 40 0.36  
 H92585, H92585 yt89c03.s1 Homo sapiens cDNA clone 231460 3'. 40 0.36  
 AA232334, AA232334 zr27b04.r1 Stratagene NT2 neuronal precurs... 40 0.36  
 N55775, N55775 J2481F Homo sapiens cDNA clone J2481 5'. 40 0.36  
 R98701, R98701 yr31f08.s1 Homo sapiens cDNA clone 206919 3'. 40 0.36  
 C14370, C14370 Human fetal brain cDNA 5'-end GEN-050F01 40 0.36  
 H19156, H19156 yn50c01.r1 Homo sapiens cDNA clone 171840 5'. 40 0.36  
 AA299557, AA299557 EST12080 Uterus tumor I Homo sapiens cDNA ... 40 0.36  
 W84460, W84460 zd89d12.r1 Soares fetal heart NbHH19W Homo sap... 40 0.36  
 T54194, T54194 ya90a02.r2 Homo sapiens cDNA clone 68906 5'. 40 0.36  
 AA100203, AA100203 zm16f12.r1 Stratagene pancreas (#937208) H... 38 1.4  
 AA993061, AA993061 ot92h08.s1 Soares\_total\_fetus\_Nb2HF8\_9w Ho... 38 1.4  
 R53406, R53406 yj70d07.r1 Homo sapiens cDNA clone 154093 5' s... 38 1.4  
 H99671, H99671 yx35b03.s1 Homo sapiens cDNA clone 263693 3'. 38 1.4  
 W03410, W03410 za07c09.r1 Soares melanocyte 2NbHM Homo sapien... 38 1.4  
 N35475, N35475 yy24b03.s1 Homo sapiens cDNA clone 272141 3'. 38 1.4  
 AA630851, AA630851 nt57f04.s1 NCI\_CGAP\_Pr3 Homo sapiens cDNA ... 38 1.4  
 N66458, N66458 yz41b08.s1 Homo sapiens cDNA clone 285591 3'. 38 1.4  
 AA736438, AA736438 zh31b09.s1 Soares pineal gland N3HPG Homo ... 38 1.4  
 AA911761, AA911761 og19b01.s1 NCI\_CGAP\_PNS1 Homo sapiens cDNA... 38 1.4  
 AA085513, AA085513 zn43a10.r1 Stratagene HeLa cell s3 937216 ... 38 1.4  
 AA678530, AA678530 ah02e05.s1 Gessler Wilms tumor Homo sapien... 38 1.4  
 AA782011, AA782011 ai75b12.s1 Soares testis NHT Homo sapiens ... 38 1.4  
 F12352, HSC38H091 H. sapiens partial cDNA sequence; clone c-... 38 1.4  
 AA861288, AA861288 ak33g01.s1 Soares testis NHT Homo sapiens ... 38 1.4  
 AA908705, AA908705 ol01b09.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 38 1.4  
 AA298850, AA298850 EST114450 Thyroid Homo sapiens cDNA 5' end 38 1.4

AA237204, AA237204 mx18d02.r1 Soares mouse NML Mus musculus c... 172 1e-41  
 AI047347, AI047347 ud65c01.y1 Sugano mouse liver mlia Mus mus... 42 0.032  
 AA832736, AA832736 vw45g10.r1 Soares mouse mammary gland NbMM... 42 0.032  
 AA960471, AA960471 vw63a05.s1 Soares mouse mammary gland NMLM... 40 0.13  
 AA880584, AA880584 vw92e01.r1 Stratagene mouse skin (#937313)... 40 0.13  
 AA107508, AA107508 mp05e07.r1 Life Tech mouse embryo 8 5dpc l... 40 0.13  
 AA116682, AA116682 mn28c06.r1 Beddington mouse embryonic regi... 40 0.13  
 AA522310, AA522310 vi45b02.r1 Beddington mouse embryonic regi... 40 0.13  
 AA162231, AA162231 mn44h02.r1 Beddington mouse embryonic regi... 40 0.13

AA414037, AA414037 vc68g03.s1 Knowles Solter mouse 2 cell Mus... 40 0.13  
 AA596585, AA596585 vm58e12.r1 Stratagene mouse Tcell 937311 M... 38 0.51  
 AA863563, AA863563 vx05a10.r1 Soares 2NbMT Mus musculus cDNA ... 38 0.51  
 AA795177, AA795177 vq94g04.r1 Knowles Solter mouse blastocyst... 38 0.51  
 AA914764, AA914764 vy92h04.r1 Soares mouse mammary gland NbMM... 38 0.51  
 AA590440, AA590440 vm20c04.r1 Knowles Solter mouse blastocyst... 38 0.51  
 AA563402, AA563402 vl75d08.r1 Knowles Solter mouse blastocyst... 38 0.51  
 AA260352, AA260352 va93c10.r1 Soares mouse 3NME12 5 Mus muscu... 38 0.51  
 AA444734, AA444734 ve75d10.r1 Soares mouse mammary gland NbMM... 38 0.51  
 C85885, C85885 Mus musculus fertilized egg cDNA 3'-end seque... 38 0.51  
 AA794590, AA794590 vu78h12.r1 Stratagene mouse skin (#937313)... 38 0.51  
 AA529643, AA529643 vi38a09.r1 Beddington mouse embryonic regi... 38 0.51  
 AA607084, AA607084 vm84a09.r1 Knowles Solter mouse blastocyst... 38 0.51  
 AA636994, AA636994 vn05g06.r1 Knowles Solter mouse blastocyst... 38 0.51  
 AA675676, AA675676 vr73h08.s1 Knowles Solter mouse 2 cell Mus... 38 0.51  
 AA163890, AA163890 ms52f09.r1 Life Tech mouse embryo 13 5dpc ... 38 0.51  
 C80539, C80539 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 38 0.51  
 AA051352, AA051352 mj53a09.r1 Soares mouse embryo NbME13.5 14... 38 0.51  
 W36885, W36885 mb64f09.r1 Soares mouse p3NMF19.5 Mus musculus... 38 0.51  
 AA930627, AA930627 vy67c05.r1 Stratagene mouse macrophage (#9... 38 0.51  
 AA244639, AA244639 mx02g12.r1 Soares mouse NML Mus musculus c... 36 2.0  
 AA967267, AA967267 vz70e08.r1 Soares mouse mammary gland NbMM... 36 2.0  
 AI048938, AI048938 uc84h06.y1 Sugano mouse kidney mkia Mus mu... 36 2.0  
 AA162722, AA162722 mn42b07.r1 Beddington mouse embryonic regi... 36 2.0  
 AA170036, AA170036 ms52d01.r1 Life Tech mouse embryo 13 5dpc ... 36 2.0  
 AA511382, AA511382 vg14b04.r1 Soares mouse NbMH Mus musculus ... 36 2.0  
 AA555634, AA555634 vk49f08.r1 Stratagene mouse Tcell 937311 M... 36 2.0  
 AA212823, AA212823 mw81c07.r1 Soares mouse NML Mus musculus c... 36 2.0  
 AA606813, AA606813 vm90h12.r1 Knowles Solter mouse blastocyst... 36 2.0  
 AA591610, AA591610 vk49d08.r1 Stratagene mouse Tcell 937311 M... 36 2.0  
 AA987039, AA987039 uc74e05.x1 Sugano mouse liver mlia Mus mus... 36 2.0  
 AA105882, AA105882 ml84h07.r1 Stratagene mouse kidney (#93731... 36 2.0  
 AA451370, AA451370 vf84h02.r1 Soares mouse mammary gland NbMM... 36 2.0  
 AA612185, AA612185 vo03d05.r1 Stratagene mouse skin (#937313)... 36 2.0  
 AA103424, AA103424 mo21e05.r1 Life Tech mouse embryo 13 5dpc ... 36 2.0  
 AA145817, AA145817 mq68a12.r1 Soares 2NbMT Mus musculus cDNA ... 36 2.0  
 AA272905, AA272905 va39d01.r1 Soares mouse 3NME12 5 Mus muscu... 36 2.0  
 AA237313, AA237313 mx17b11.r1 Soares mouse NML Mus musculus c... 36 2.0  
 AA267119, AA267119 mz74d07.r1 Soares mouse lymph node NbMLN M... 36 2.0  
 AA106683, AA106683 ml83h06.r1 Stratagene mouse kidney (#93731... 36 2.0  
 AA125061, AA125061 mq83d10.r1 Stratagene mouse melanoma (#937... 36 2.0  
 AA655241, AA655241 vq84c07.s1 Knowles Solter mouse 2 cell Mus... 36 2.0  
 AA512835, AA512835 vg13f11.r1 Soares mouse NbMH Mus musculus ... 36 2.0

C70525, C70525 *C.elegans* cDNA clone yk409g6 : 5' end, single... 44 0.007  
 F15112, SSO4D09 *S.scrofa* mRNA; expressed sequence tag (5'; c... 42 0.029  
 AA684640, AA684640 EST104989 Rat PC-12 cells, untreated Rattu... 40 0.11  
 H32045, H32045 EST106774 Rat PC-12 cells, untreated Rattus sp... 40 0.11  
 AA660422, AA660422 00298 *MtRHE* *Medicago truncatula* cDNA 5' 40 0.11  
 C59696, C59696 *C.elegans* cDNA clone yk440e1 : 3' end, single... 38 0.45  
 AI008699, AI008699 EST203150 Normalized rat embryo, Bento Soa... 38 0.45  
 AA753263, AA753263 96BS0294 Rice Immature Seed Lambda ZAPII c... 38 0.45  
 T38461, T38461 EST103957 *Saccharomyces cerevisiae* cDNA 3' end. 38 0.45  
 C59257, C59257 *C.elegans* cDNA clone yk386b12 : 3' end, singl... 38 0.45  
 AA948906, AA948906 LD27590.5prime LD *Drosophila melanogaster* ... 38 0.45  
 AI001628, AI001628 EST0210 *Tilapia* brain cDNA library in pUC1... 38 0.45  
 H31962, H31962 EST106545 Rat PC-12 cells, untreated Rattus sp... 38 0.45  
 AA979509, AA979509 LD34118.5prime LD *Drosophila melanogaster* ... 38 0.45  
 D41274, RICS3647A Rice cDNA, partial sequence (S3647\_1A). 38 0.45  
 C58362, C58362 *C.elegans* cDNA clone yk366a8 : 3' end, single... 38 0.45  
 C57756, C57756 *C.elegans* cDNA clone yk298b9 : 3' end, single... 38 0.45  
 AA753070, AA753070 97AS2091 Rice Immature Seed Lambda ZAPII c... 38 0.45  
 H74687, H74687 383 *Brassica napus* cDNA clone R25R. 38 0.45  
 C10513, C10513 *C.elegans* cDNA clone yk147e9 : 3' end, single... 38 0.45  
 C55569, C55569 *C.elegans* cDNA clone yk191d1 : 3' end, single... 38 0.45  
 C94819, C94819 *Sus scrofa* mRNA; expressed sequence tag (5'; ... 38 0.45  
 C32982, C32982 *C.elegans* cDNA clone yk338a12 : 3' end, singl... 38 0.45  
 AA816691, AA816691 LD03795.5prime LD *Drosophila melanogaster* ... 36 1.8  
 AA519844, AA519844 TgESTzz36c03.r1 TgME49 invivo Bradyzoite c... 36 1.8  
 AA531839, AA531839 TgESTzz47h05.r1 TgME49 invivo Bradyzoite c... 36 1.8  
 AA660182, AA660182 00022 *MtRHE* *Medicago truncatula* cDNA 5' si... 36 1.8  
 D71983, CELK084H2R *C.elegans* cDNA clone yk84h2 : 3' end, sin... 36 1.8  
 R29905, R29905 12510 Lambda-PRL2 *Arabidopsis thaliana* cDNA cl... 36 1.8  
 AA519997, AA519997 TgESTzz36h03.r1 TgME49 invivo Bradyzoite c... 36 1.8  
 U83048, BTU83048 *Bos taurus* clone 0429 mRNA sequence 36 1.8  
 AA440655, AA440655 LD15510.5prime LD *Drosophila melanogaster* ... 36 1.8  
 AA559374, AA559374 MU002092.NH3 York-Harrop-lung-A *Schistosom*... 36 1.8  
 C93857, C93857 *Dictyostelium discoideum* slug cDNA, clone SSL794 36 1.8  
 AA520901, AA520901 TgESTzz65a05.r1 TgME49 invivo Bradyzoite c... 36 1.8  
 T46158, T46158 9421 Lambda-PRL2 *Arabidopsis thaliana* cDNA clo... 36 1.8  
 AA520866, AA520866 TgESTzz68e05.r1 TgME49 invivo Bradyzoite c... 36 1.8  
 Z17562, ATTS0136 *A. thaliana* transcribed sequence; clone TAT... 36 1.8  
 AA520811, AA520811 TgESTzz64d05.r1 TgME49 invivo Bradyzoite c... 36 1.8  
 AA567455, AA567455 HL01288.5prime HL *Drosophila melanogaster* ... 36 1.8  
 AA519228, AA519228 TgESTzz39h02.s1 TgME49 invivo Bradyzoite c... 36 1.8  
 AA531917, AA531917 TgESTzz48f01.r1 TgME49 invivo Bradyzoite c... 36 1.8  
 AA519829, AA519829 TgESTzz36a02.r1 TgME49 invivo Bradyzoite c... 36 1.8  
 AA520185, AA520185 TgESTzz39d03.s1 TgME49 invivo Bradyzoite c... 36 1.8  
 C37095, C37095 *C.elegans* cDNA clone yk482c11 : 3' end, singl... 36 1.8

T46009, T46009	9272	Lambda-PRL2	Arabidopsis thaliana cDNA clo...	36	1.8
T20458, T20458	2466	Lambda-PRL2	Arabidopsis thaliana cDNA clo...	36	1.8
F14402, ATTS5324			A. thaliana transcribed sequence; clone TAP...	36	1.8
T20404, T20404	2412	Lambda-PRL2	Arabidopsis thaliana cDNA clo...	36	1.8
AA274295, AA274295		TgESTzz24c11.s1	TgME49 invivo Bradyzoite c...	36	1.8
AA699152, AA699152		HL07807.5prime	HL Drosophila melanogaster ...	36	1.8
AA902065, AA902065		NCM1A12T3	Mycelial Neurospora crassa cDNA ...	36	1.8

SEQ ID NO:558

AF016585, AF016585	<i>Streptomyces caelestis</i> cytochrome P-450 hy...	42	0.092
U50719, MSU50719	<i>Manduca sexta</i> neuroglian mRNA, complete cds	40	0.36
Z97208, SPAC15A10	<i>S.pombe</i> chromosome I cosmid c15A10	40	0.36
AC003063, AC003063	<i>Mus musculus</i> Chromosome 16 BAC Clone b40-o...	40	0.36
X66455, MMFGFR2	<i>M.musculus</i> promoter region of fibroblast gro...	40	0.36
D83785, D83785	Human mRNA for KIAA0200 gene, complete cds	40	0.36
AC000398, AC000398	Genomic sequence from Mouse 11, complete s...	38	1.4
AF062345, AF062345	<i>Caulobacter crescentus</i> Sts1 (sts1), S-laye...	38	1.4
X12359, RCNIFR12	<i>Rhodobacter capsulatus</i> nifR1 and nifR2 gene	38	1.4
X72382, RCNIFR3	<i>R.capsulatus</i> nifR3 DNA	38	1.4

## HUMAN ESTs

R36714, R36714 yh93g06.s1 Homo sapiens cDNA clone 137338 3'. 775 0.0  
D61030, HUM149A04B Human fetal brain cDNA 5'-end GEN-149A04. 666 0.0  
D60944, HUM141D02B Human fetal brain cDNA 5'-end GEN-141D02. 656 0.0  
H03308, H03308 yj47d09.s1 Homo sapiens cDNA clone 151889 3'. 609 e-172  
AA435561, AA435561 zt73d09.s1 Soares testis NHT Homo sapiens ... 587 e-166  
AA977877, AA977877 oq56d03.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 571 e-161  
AA846787, AA846787 aj41h03.s1 Soares testis NHT Homo sapiens ... 563 e-159  
AA972542, AA972542 oo82e01.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 561 e-158  
AA954270, AA954270 on72e06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 557 e-157  
AA740333, AA740333 ob23c02.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 557 e-157  
AA999722, AA999722 ov04c06.s1 NCI\_CGAP\_Kid3 Homo sapiens cDNA... 555 e-156  
AA970621, AA970621 op40h08.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 551 e-155  
AA932930, AA932930 oo04g11.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 541 e-152  
AA725406, AA725406 ai13b11.s1 Soares parathyroid tumor NbHPA ... 539 e-152  
W74439, W74439 zd75d10.s1 Soares fetal heart NbHH19W Homo sap... 539 e-152  
AA868538, AA868538 ak43e08.s1 Soares testis NHT Homo sapiens ... 539 e-152  
R79832, R79832 yi89b08.s1 Homo sapiens cDNA clone 146391 3' s... 537 e-151



R63227, R63227 yi07e06.s1 Homo sapiens cDNA clone 138562 3'. 535 e-150  
 AI027967, AI027967 ov84d04.x1 Soares\_testis\_NHT Homo sapiens ... 535 e-150  
 AA776717, AA776717 ah49d07.s1 Soares testis NHT Homo sapiens ... 535 e-150  
 AI040961, AI040961 ov53d06.x1 Soares\_testis\_NHT Homo sapiens ... 533 e-150  
 AI024835, AI024835 ov35h09.x1 Soares\_testis\_NHT Homo sapiens ... 533 e-150  
 AA740667, AA740667 ob01g12.s1 NCI\_CGAP\_Kid3 Homo sapiens cDNA... 531 e-149  
 AA994527, AA994527 ou42h06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 531 e-149  
 AA932728, AA932728 oo31g06.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 529 e-149  
 AI001978, AI001978 ot39f03.s1 Soares\_testis\_NHT Homo sapiens ... 529 e-149  
 N37092, N37092 yy41g08.s1 Homo sapiens cDNA clone 273854 3'. 529 e-149  
 N27547, N27547 yy01e05.s1 Homo sapiens cDNA clone 269984 3'. 527 e-148  
 AA883578, AA883578 al46b08.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 527 e-148  
 AA890154, AA890154 al53f07.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 525 e-147  
 AA757222, AA757222 ah56f11.s1 Soares testis NHT Homo sapiens ... 525 e-147  
 AA456074, AA456074 aa17b07.s1 Soares\_NhHMPu\_S1 Homo sapiens c... 523 e-147  
 AA884285, AA884285 am32f04.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 523 e-147  
 AA969436, AA969436 op53e12.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 521 e-146  
 AA952918, AA952918 on55h11.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 521 e-146  
 AA971938, AA971938 op88b01.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 521 e-146  
 R25112, R25112 yh36b12.s1 Homo sapiens cDNA clone 131807 3'. 519 e-146  
 AA865258, AA865258 og87d08.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 519 e-146  
 AA758323, AA758323 ah65e11.s1 Soares testis NHT Homo sapiens ... 519 e-146  
 AA972041, AA972041 op88e06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 519 e-146  
 R76443, R76443 yi58e11.s1 Homo sapiens cDNA clone 143468 3'. 519 e-146  
 AA917965, AA917965 om37e04.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 517 e-145  
 AA505880, AA505880 ni01a09.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 517 e-145  
 AA906270, AA906270 oj98e12.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 517 e-145  
 AA758549, AA758549 ah70b04.s1 Soares testis NHT Homo sapiens ... 517 e-145  
 AA927156, AA927156 om20f05.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 515 e-144  
 AA976254, AA976254 oo30f08.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 515 e-144  
 R23891, R23891 yh28a12.s1 Homo sapiens cDNA clone 131038 3'. 515 e-144  
 AA938552, AA938552 oo78g11.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 513 e-144  
 AA483809, AA483809 ne41c08.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 513 e-144  
 AA962659, AA962659 or31f10.s1 NCI\_CGAP\_GC3 Homo sapiens cDNA ... 511 e-143  
 AA724803, AA724803 ai05f02.s1 Soares parathyroid tumor NbHPA ... 511 e-143  
 AA410432, AA410432 zv12c09.s1 Soares\_NhHMPu\_S1 Homo sapiens c... 511 e-143  
 AA775373, AA775373 ad19c07.s1 Soares\_NbHFB Homo sapiens cDNA ... 511 e-143  
 AA758038, AA758038 ah67h09.s1 Soares testis NHT Homo sapiens ... 509 e-143  
 AA904368, AA904368 ol15d02.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 509 e-143  
 AA861386, AA861386 ak37b11.s1 Soares testis NHT Homo sapiens ... 507 e-142  
 R31547, R31547 yh72g03.s1 Homo sapiens cDNA clone 135316 3'. 505 e-141  
 AA843421, AA843421 ak07f11.s1 Soares parathyroid tumor NbHPA ... 504 e-141  
 H02479, H02479 yj35e10.s1 Homo sapiens cDNA clone 150762 3'. 504 e-141  
 N29346, N29346 yw85c12.s1 Homo sapiens cDNA clone 259030 3'. 504 e-141  
 AA815351, AA815351 ai63g05.s1 Soares testis NHT Homo sapiens ... 504 e-141

AA923373, AA923373 ol46e03.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 502 e-140  
H01218, H01218 yj31c08.s1 Homo sapiens cDNA clone 150350 3'. 500 e-140  
AA988977, AA988977 or87e11.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 500 e-140  
AA628621, AA628621 af40c02.s1 Soares total fetus Nb2HF8 9w Ho... 500 e-140  
AA442745, AA442745 zv60a07.s1 Soares testis NHT Homo sapiens ... 498 e-139  
AA777492, AA777492 zj02e07.s1 Soares fetal liver spleen 1NFLS... 498 e-139  
R73670, R73670 yi55f03.s1 Homo sapiens cDNA clone 143165 3'. 498 e-139  
H12460, H12460 yj12d05.s1 Homo sapiens cDNA clone 148521 3'. 498 e-139  
AA875917, AA875917 oj15a08.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 496 e-138  
R76230, R76230 yi71g11.s1 Homo sapiens cDNA clone 144740 3'. 494 e-138  
AA970616, AA970616 op40h03.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 494 e-138  
AA912408, AA912408 ol23a05.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 492 e-137  
AA910051, AA910051 ol40e08.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 492 e-137  
AA815444, AA815444 ai65b11.s1 Soares testis NHT Homo sapiens ... 492 e-137  
R76814, R76814 yi62f06.s1 Homo sapiens cDNA clone 143843 3'. 488 e-136  
AA954722, AA954722 oo84c12.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 488 e-136  
R65987, R65987 yi23e10.s1 Homo sapiens cDNA clone 140106 3'. 486 e-136  
R63480, R63480 yi08e11.s1 Homo sapiens cDNA clone 138668 3'. 486 e-136  
AA885425, AA885425 am12h09.s1 Soares NFL T GBC S1 Homo sapien... 486 e-136  
AA884231, AA884231 am32a01.s1 Soares NFL T GBC S1 Homo sapien... 484 e-135  
AA885048, AA885048 am11a12.s1 Soares NFL T GBC S1 Homo sapien... 482 e-134  
AA996162, AA996162 os14f10.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 482 e-134  
AA748637, AA748637 ny10a02.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 482 e-134  
AI031908, AI031908 ow47e12.x1 Soares\_parathyroid\_tumor\_NbHPA ... 482 e-134  
AA884703, AA884703 am18e02.s1 Soares NFL T GBC S1 Homo sapien... 480 e-134  
AA928243, AA928243 on87c10.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 480 e-134  
AI025986, AI025986 ow03a09.s1 Soares\_parathyroid\_tumor\_NbHPA ... 478 e-133  
AA897637, AA897637 oj72g07.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 472 e-131  
AA877346, AA877346 olc07.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 472 e-131  
AA833569, AA833569 aj46b02.s1 Soares testis NHT Homo sapiens ... 472 e-131  
AA832163, AA832163 oc91b02.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 470 e-131  
R89052, R89052 ym99e08.s1 Homo sapiens cDNA clone 167078 3'. 470 e-131  
N26589, N26589 yx91f03.s1 Homo sapiens cDNA clone 269117 3'. 460 e-128  
R73883, R73883 yi56c03.s1 Homo sapiens cDNA clone 143236 3'. 454 e-126  
AA579968, AA579968 ng51c03.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 444 e-123  
AA843427, AA843427 ak07g06.s1 Soares parathyroid tumor NbHPA ... 438 e-121  
AA705903, AA705903 ah42g12.s1 Soares testis NHT Homo sapiens ... 436 e-121  
AA835882, AA835882 oc81d05.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 434 e-120  
AA812583, AA812583 aj43b02.s1 Soares testis NHT Homo sapiens ... 432 e-119  
AA512970, AA512970 nj16b08.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 432 e-119  
R26664, R26664 yh35g10.s1 Homo sapiens cDNA clone 131778 3'. 428 e-118  
AA429715, AA429715 zv60a07.r1 Soares testis NHT Homo sapiens ... 414 e-114  
H17430, H17430 ym40f09.s1 Homo sapiens cDNA clone 50607 3'. 404 e-111  
AA436117, AA436117 zu03d10.r1 Soares testis NHT Homo sapiens ... 402 e-110  
AA099077, AA099077 zl77a09.s1 Stratagene colon (#937204) Homo... 400 e-110

R72440, R72440 yj90h02.s1 Homo sapiens cDNA clone 156051 3'. 379 e-103  
 AA577436, AA577436 nm96h06.s1 NCI\_CGAP\_Co9 Homo sapiens cDNA ... 351 4e-95  
 AA516390, AA516390 nf55e03.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 347 6e-94  
 AA534533, AA534533 nf80h06.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 341 3e-92  
 AA541583, AA541583 ni89f05.s1 NCI\_CGAP\_Pr21 Homo sapiens cDNA... 311 3e-83  
 N72191, N72191 yz99f07.s1 Homo sapiens cDNA clone 291205 3'. 303 8e-81  
 AA905015, AA905015 ok09b08.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 303 8e-81  
 AA393148, AA393148 zt73d09.r1 Soares testis NHT Homo sapiens ... 287 4e-76  
 AA939048, AA939048 op56h04.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 256 2e-66  
 AA412317, AA412317 zt97c05.r1 Soares testis NHT Homo sapiens ... 246 2e-63  
 R65986, R65986 yi23e10.r1 Homo sapiens cDNA clone 140106 5'. 238 4e-61  
 AA400827, AA400827 zt76c07.s1 Soares testis NHT Homo sapiens ... 232 2e-59  
 W00472, W00472 yz99f07.r1 Homo sapiens cDNA clone 291205 5'. 180 8e-44  
 AA860558, AA860558 aj81e09.s1 Soares parathyroid tumor NbHPA ... 180 8e-44  
 AA455577, AA455577 aa17b07.r1 Soares NhHMPu S1 Homo sapiens c... 176 1e-42  
 AA583931, AA583931 nn64e04.s1 NCI\_CGAP\_Lar1 Homo sapiens cDNA... 172 2e-41  
 AA907332, AA907332 ol22g11.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 168 3e-40  
 R71169, R71169 yi53a12.r1 Homo sapiens cDNA clone 142942 5'. 159 3e-37  
 W79084, W79084 zd75d10.r1 Soares fetal heart NbHH19W Homo sap... 155 4e-36  
 AA295914, AA295914 EST101137 Thymus III Homo sapiens cDNA 5' end 135 4e-30  
 AA860415, AA860415 aj60d10.s1 Soares testis NHT Homo sapiens ... 100 2e-19  
 H01351, H01351 yi99a07.r1 Homo sapiens cDNA clone 147348 5'. 98 9e-19  
 AA709286, AA709286 ai21g07.s1 Soares testis NHT Homo sapiens ... 96 3e-18  
 AA931370, AA931370 oo03d01.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 96 3e-18  
 AA501911, AA501911 ng54a08.s1 NCI\_CGAP\_Li2 Homo sapiens cDNA ... 94 1e-17  
 AA548419, AA548419 nj14g09.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 92 5e-17  
 AA588892, AA588892 no23b06.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 92 5e-17  
 AI025228, AI025228 ov40h08.x1 Soares\_testis\_NHT Homo sapiens ... 76 3e-12  
 R73757, R73757 yi55f03.r1 Homo sapiens cDNA clone 143165 5'. 74 1e-11  
 R23710, R23710 yh35g10.r1 Homo sapiens cDNA clone 131778 5'. 56 3e-06  
 N40362, N40362 yy01e05.r1 Homo sapiens cDNA clone 269984 5'. 50 2e-04  
 H59895, H59895 yr04c12.r1 Homo sapiens cDNA clone 204310 5'. 48 7e-04  
 H12509, H12509 yj12d05.r1 Homo sapiens cDNA clone 148521 5'. 44 0.011  
 N20344, N20344 yx38d02.s1 Homo sapiens cDNA clone 264003 3'. 38 0.70  
 AA614692, AA614692 np52b10.s1 NCI\_CGAP\_Br1.1 Homo sapiens cDN... 38 0.70  
 H30707, H30707 yo78f07.r1 Homo sapiens cDNA clone 184069 5'. 36 2.7  
 H52973, H52973 yq82e04.r1 Homo sapiens cDNA clone 202302 5'. 36 2.7  
 AA218550, AA218550 zq96b02.r1 Stratagene NT2 neuronal precurs... 36 2.7  
 AA312481, AA312481 EST183215 Jurkat T-cells VI Homo sapiens c... 36 2.7  
 AA632009, AA632009 np74c07.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 36 2.7  
 H13363, H13363 yl71b10.r1 Homo sapiens cDNA clone 43343 5'. 36 2.7  
 AI022018, AI022018 ow64d01.x1 Soares\_senescent\_fibroblasts\_Nb... 36 2.7  
 AA781996, AA781996 ai75a06.s1 Soares testis NHT Homo sapiens ... 36 2.7  
 N21623, N21623 yx60a09.s1 Homo sapiens cDNA clone 266104 3'. 36 2.7  
 AA326194, AA326194 EST29340 Cerebellum II Homo sapiens cDNA 5... 36 2.7

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C76071, C76071 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 250 4e-65  
 AA051612, AA051612 mj52c07.r1 Soares mouse embryo NbME13.5 14... 238 1e-61  
 AA561635, AA561635 vl01h07.r1 Knowles Solter mouse blastocyst... 234 2e-60  
 AA288419, AA288419 vb14h01.r1 Soares mouse NML Mus musculus c... 220 3e-56  
 AA212883, AA212883 mw78e10.r1 Soares mouse NML Mus musculus c... 220 3e-56  
 AA268018, AA268018 vb08e07.r1 Soares mouse NML Mus musculus c... 212 8e-54  
 AA692427, AA692427 vt59b07.r1 Barstead mouse irradiated colon... 200 3e-50  
 W18566, W18566 mb98h02.r1 Soares mouse p3NMF19.5 Mus musculus... 192 7e-48  
 AA543948, AA543948 vj69b08.r1 Knowles Solter mouse blastocyst... 147 4e-34  
 W41070, W41070 mc39b06.r1 Soares mouse p3NMF19.5 Mus musculus... 123 5e-27  
 Z31174, MMTEST52 M.musculus expressed sequence tag MTEST52 117 3e-25  
 AA530723, AA530723 vj32f07.r1 Stratagene mouse diaphragm (#93... 74 5e-12  
 AA966940, AA966940 ua38c01.r1 Soares mouse mammary gland NbMM... 72 2e-11  
 AA111079, AA111079 mp50e01.r1 Barstead MPLRB1 Mus musculus cD... 44 0.004  
 AA049187, AA049187 mj51a02.r1 Soares mouse embryo NbME13.5 14... 36 0.99  
 AA058246, AA058246 mg74e12.r1 Soares mouse embryo NbME13.5 14... 36 0.99  
 AA153730, AA153730 mq60a02.r1 Soares 2NbMT Mus musculus cDNA ... 36 0.99  
 AA473959, AA473959 vd02b12.s1 Knowles Solter mouse 2 cell Mus... 36 0.99  
 W47887, W47887 mc83h09.r1 Soares mouse embryo NbME13.5 14.5 M... 36 0.99  
 AA033312, AA033312 mi43g01.r1 Soares mouse embryo NbME13.5 14... 36 0.99  
 AA980820, AA980820 ua46a04.r1 Soares mouse mammary gland NbMM... 36 0.99  
 Z31139, MMTEST427 M.musculus expressed sequence tag MTEST427 36 0.99  
 C76637, C76637 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 34 3.9  
 AI049314, AI049314 uc87b10.y1 Sugano mouse kidney mkia Mus mu... 34 3.9  
 AA670807, AA670807 vs70b02.r1 Stratagene mouse skin (#937313)... 34 3.9  
 AA727571, AA727571 vv01h11.r1 Stratagene mouse skin (#937313)... 34 3.9  
 AA571966, AA571966 vg12f07.r1 Soares mouse NbMH Mus musculus ... 34 3.9  
 W37059, W37059 mb73f10.r1 Soares mouse p3NMF19.5 Mus musculus... 34 3.9  
 AA760280, AA760280 vv74h11.r1 Stratagene mouse skin (#937313)... 34 3.9  
 AA799036, AA799036 vn40c12.r1 Stratagene mouse skin (#937313)... 34 3.9  
 AA432831, AA432831 vf28g07.r1 Knowles Solter mouse 8 cell Mus... 34 3.9  
 AA562435, AA562435 vk98c01.r1 Knowles Solter mouse blastocyst... 34 3.9  
 AA726680, AA726680 vu93g12.r1 Stratagene mouse skin (#937313)... 34 3.9  
 AA217464, AA217464 mu87d11.r1 Soares mouse lymph node NbMLN M... 34 3.9  
 AA790564, AA790564 vx71e06.r1 Stratagene mouse skin (#937313)... 34 3.9  
 AA033172, AA033172 mi37f06.r1 Soares mouse embryo NbME13.5 14... 34 3.9  
 AA616204, AA616204 vo96h02.r1 Soares mouse mammary gland NbMM... 34 3.9  
 AA982055, AA982055 ua37h05.r1 Soares mouse mammary gland NbMM... 34 3.9  
 W47850, W47850 mc82h10.r1 Soares mouse embryo NbME13.5 14.5 M... 34 3.9  
 AA537538, AA537538 vk48c12.r1 Soares mouse mammary gland NbMM... 34 3.9  
 AA636986, AA636986 vn05f04.r1 Knowles Solter mouse blastocyst... 34 3.9

AI043768, AI043768 UI-R-C0-jm-d-11-0-UI.s1 UI-R-C0 Rattus nor... 174 1e-42  
 AA531635, AA531635 TgESTzz29b08.r1 TgME49 invivo Bradyzoite c... 38 0.22  
 AA944260, AA944260 EST199759 Normalized rat embryo, Bento Soa... 38 0.22  
 AI008930, AI008930 EST203381 Normalized rat embryo, Bento Soa... 36 0.87  
 D15788, RICC1258A Rice cDNA, partial sequence (C1258A). 36 0.87  
 AA963741, AA963741 UI-R-C0-gt-b-09-0-UI.s1 UI-R-C0 Rattus nor... 36 0.87  
 AA951235, AA951235 LD31601.3prime LD Drosophila melanogaster ... 34 3.5  
 C20118, C20118 Rice cDNA, partial sequence (E11542\_2A) 34 3.5  
 AA820317, AA820317 LD23876.5prime LD Drosophila melanogaster ... 34 3.5  
 AA950448, AA950448 LD30237.3prime LD Drosophila melanogaster ... 34 3.5

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U83883, RNU83883 Rattus norvegicus p105 coactivator mRNA, com... 42 0.11  
 V00722, MMBGL1 Mouse gene for beta-1-globin. 40 0.45  
 X14061, MMBGCXD M.musculus beta-globin complex DNA for y, bh... 40 0.45  
 U20824, EHVU20824 Equine herpesvirus 2, complete genome 38 1.8  
 U04106, PFU04106 Pleurotus fossulatus D1822, mating group VI,... 38 1.8  
 U04101, POU04101 Pleurotus ostreatus D1742, Japan, mating gro... 38 1.8  
 AC005174, AC005174 Homo sapiens clone UWGC:g1564a012 from 7p1... 38 1.8  
 M18680, HUMRGAPS Homo sapiens 5S rRNA pseudogene. 38 1.8  
 AL022121, MTV025 Mycobacterium tuberculosis H37Rv complete g... 38 1.8  
 AF038379, AF038379 Leishmania amazonensis ribosomal protein S... 38 1.8  
 Z11528, THIGPMR T.harzianum mRNA for imidazoleglycerolphosphate 38 1.8  
 U32622, CTU32622 Comamonas testosteroni TsaR (tsaR), toluenes... 38 1.8  
 U04102, POU04102 Pleurotus ostreatus D1743, Japan, mating gro... 38 1.8  
 U04105, PFU04105 Pleurotus fossulatus D1821, mating group VI,... 38 1.8  
 U04109, PEU04109 Pleurotus eryngii D1832, mating group VI rib... 38 1.8  
 U65606, BSU65606 Basidiomycete from a bamboo (Phyllostachys p... 38 1.8

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R49969, R49969 yj56c07.s1 Homo sapiens cDNA clone 152748 3' s... 523 e-147  
 AA834501, AA834501 of21c02.s1 NCI\_CGAP\_Kid6 Homo sapiens cDNA... 381 e-104  
 W96422, W96422 ze43a05.s1 Soares retina N2b4HR Homo sapiens c... 315 2e-84  
 R47821, R47821 yj56c07.r1 Homo sapiens cDNA clone 152748 5'. 214 7e-54  
 AA761660, AA761660 nz24b09.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 212 3e-53  
 AA887861, AA887861 nq99b07.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 74 2e-11  
 AA644044, AA644044 nm20b12.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 72 6e-11

AA115963, AA115963 zm78d11.s1 Stratagene neuroepithelium (#93... 40 0.22  
AA779271, AA779271 zj43f02.s1 Soares fetal liver spleen 1NFLS... 40 0.22  
T65600, T65600 yc76a04.r1 Homo sapiens cDNA clone 21496 5'. 38 0.86  
AA515882, AA515882 nf67f10.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 38 0.86  
AA664812, AA664812 nu69b05.s1 NCI\_CGAP\_Alv1 Homo sapiens cDNA... 36 3.4  
T83365, T83365 ye03f05.s1 Homo sapiens cDNA clone 116673 3'. 36 3.4  
AA009773, AA009773 zi04d04.s1 Soares fetal liver spleen 1NFLS... 36 3.4  
AA916894, AA916894 og34g10.s1 NCI\_CGAP\_Br7 Homo sapiens cDNA ... 36 3.4  
N27865, N27865 yy02g03.s1 Homo sapiens cDNA clone 270100 3'. 36 3.4  
AA953544, AA953544 om79g06.s1 NCI\_CGAP\_Kid3 Homo sapiens cDNA... 36 3.4  
AA505576, AA505576 nh93f03.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 36 3.4  
H30276, H30276 yp42f05.s1 Homo sapiens cDNA clone 190113 3'. 36 3.4  
AA699914, AA699914 zi61f08.s1 Soares fetal liver spleen 1NFLS... 36 3.4  
AA595583, AA595583 nk92c04.s1 NCI\_CGAP\_Co11 Homo sapiens cDNA... 36 3.4  
AA351139, AA351139 EST58769 Infant brain Homo sapiens cDNA 5'... 36 3.4  
AA810167, AA810167 ob88a03.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 36 3.4  
H50257, H50257 yo28a07.r1 Homo sapiens cDNA clone 179220 5'. 36 3.4  
W19939, W19939 zb37e09.r1 Soares parathyroid tumor NbHPA Homo... 36 3.4  
R19840, R19840 yg30e11.r1 Homo sapiens cDNA clone 33837 5'. 36 3.4  
AA514234, AA514234 nf56e10.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 36 3.4

AA183407, AA183407 ms  
AA821640, AA821640 vw  
AA289310, AA289310

AA900756, AA900756 UI-R-E0-di-d-04-0-UI.s1 UI-R-E0 Rattus nor... 46 0.001  
T18416, T18416 6c02e07t7 etiolated seedling Zea mays cDNA clo... 40 0.069  
AA817427, AA817427 LD22827.5prime LD Drosophila melanogaster ... 36 1.1  
AA274351, AA274351 TgESTzz25c09.s1 TgME49 invivo Bradyzoite c... 36 1.1  
AA391823, AA391823 LD10747.5prime LD Drosophila melanogaster ... 36 1.1  
AA274275, AA274275 TgESTzz24b02.s1 TgME49 invivo Bradyzoite c... 34 4.3  
R86490, R86490 RABEST068T Oryctolagus cuniculus cDNA clone pR... 34 4.3  
AA965817, AA965817 o5g08a1.r1 Aspergillus nidulans 24hr asexu... 34 4.3

SEQ ID NO:560

X81198, L35746, L49403, U21317, Z35640, AL010273, U09850, AF071771, Z96434,

Z50028, X72735, U13072, Z34294, AB002109, X68401, M92840, D88399, Z36238, AF000262, Z46828,

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AA215808, AA215808 zr98b10.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 1082 0.0  
 N75131, N75131 yz29g07.r1 Soares multiple sclerosis 2NbHMSP H... 989 0.0  
 AA709149, AA709149 zf98g05.s1 Soares fetal heart NbHH19W Homo... 985 0.0  
 AA428341, AA428341 zw18f09.s1 Soares ovary tumor NbHOT Homo s... 967 0.0  
 AA043426, AA043426 zk54h09.r1 Soares pregnant uterus NbHPU Ho... 870 0.0  
 AA878521, AA878521 oj19c01.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 844 0.0  
 AA599696, AA599696 ag10h01.s1 Gessler Wilms tumor Homo sapien... 842 0.0  
 W52304, W52304 zc47c08.r1 Soares senescent fibroblasts NbHSF ... 841 0.0  
 AA043427, AA043427 zk54h09.s1 Soares pregnant uterus NbHPU Ho... 769 0.0  
 N64314, N64314 yz46a12.s1 Homo sapiens cDNA clone 286078 3'. 763 0.0  
 N52360, N52360 yz29g07.s1 Soares multiple sclerosis 2NbHMSP H... 753 0.0  
 AA290863, AA290863 zt19a08.s1 Soares ovary tumor NbHOT Homo s... 747 0.0  
 AA768023, AA768023 oa60e03.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 728 0.0  
 AA872018, AA872018 oi05f08.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 718 0.0  
 AA164765, AA164765 zp01g09.s1 Stratagene ovarian cancer (#937... 716 0.0  
 AA814881, AA814881 oa75e02.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 708 0.0  
 R86915, R86915 yq30f07.r1 Homo sapiens cDNA clone 197317 5'. 692 0.0  
 W56703, W56703 zd14e01.r1 Soares fetal heart NbHH19W Homo sap... 642 0.0  
 R84872, R84872 yq27e01.r1 Soares fetal liver spleen 1NFLS Hom... 636 0.0  
 D79691, HUM307D10B Human aorta cDNA 5'-end GEN-307D10. 630 e-179  
 AA025638, AA025638 ze90d11.s1 Soares fetal heart NbHH19W Homo... 626 e-178  
 AA298883, AA298883 EST114512 Pancreas tumor I Homo sapiens cD... 624 e-177  
 R86903, R86903 yq30d07.r1 Homo sapiens cDNA clone 197293 5'. 622 e-176  
 AA033584, AA033584 zk21b12.s1 Soares pregnant uterus NbHPU Ho... 618 e-175  
 AA633335, AA633335 nq58h09.s1 NCI\_CGAP\_Co9 Homo sapiens cDNA ... 611 e-173  
 AA298894, AA298894 EST114513 Pancreas tumor I Homo sapiens cD... 599 e-169  
 R85806, R85806 yq27e01.s1 Soares fetal liver spleen 1NFLS Hom... 595 e-168  
 AA872617, AA872617 oi05g07.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 591 e-167  
 H71458, H71458 yu71a06.s1 Homo sapiens cDNA clone 239218 3'. 587 e-166  
 AA291045, AA291045 zt19a08.r1 Soares ovary tumor NbHOT Homo s... 563 e-159  
 H71587, H71587 yu71a06.r1 Homo sapiens cDNA clone 239218 5'. 543 e-153  
 AA035172, AA035172 zk28g05.s1 Soares pregnant uterus NbHPU Ho... 523 e-147  
 AA164764, AA164764 zp01g09.r1 Stratagene ovarian cancer (#937... 517 e-145  
 AA297001, AA297001 EST112550 Adipose tissue, white II Homo sa... 502 e-140  
 AA296816, AA296816 EST112381 Aorta endothelial cells Homo sap... 500 e-139  
 AA769090, AA769090 oa74e12.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 494 e-138  
 H54447, H54447 yq91f04.s1 Homo sapiens cDNA clone 203167 3'. 438 e-121  
 H54537, H54537 yq91f04.r1 Homo sapiens cDNA clone 203167 5'. 436 e-120  
 AI049757, AI049757 an26g03.x1 Gessler Wilms tumor Homo sapien... 430 e-119

AA033583, AA033583 zk21b12.r1 Soares pregnant uterus NbHPU Ho... 422 e-116  
D61748, HUM205G02B Human aorta cDNA 5'-end GEN-205G02. 412 e-113  
AA148635, AA148635 zl26d10.r1 Soares pregnant uterus NbHPU Ho... 377 e-102  
AA148636, AA148636 zl26d10.s1 Soares pregnant uterus NbHPU Ho... 373 e-101  
AA025637, AA025637 ze90d11.r1 Soares fetal heart NbHH19W Homo... 371 e-101  
AA932620, AA932620 oo61h04.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 365 4e-99  
AA385594, AA385594 EST99296 Thyroid Homo sapiens cDNA 5' end 339 2e-91  
AA361957, AA361957 EST71295 T-cell lymphoma Homo sapiens cDNA... 289 2e-76  
AA383998, AA383998 EST97483 Thyroid Homo sapiens cDNA 5' end ... 274 1e-71  
H22175, H22175 yl38a03.r1 Homo sapiens cDNA clone 160492 5'. 256 3e-66  
R50060, R50060 yj59c10.r1 Homo sapiens cDNA clone 153042 5'. 256 3e-66  
AA229414, AA229414 nc47f12.r1 NCI\_CGAP\_Pr3 Homo sapiens cDNA ... 246 3e-63  
D20466, HUMGS01440 Human HL60 3'directed MboI cDNA, HUMGS014... 208 6e-52  
AA249061, AA249061 ll4438.seq.F Human fetal heart, Lambda ZAP... 168 5e-40  
R86758, R86758 yq30f07.s1 Homo sapiens cDNA clone 197317 3'. 147 2e-33  
R58025, R58025 F8018 Fetal heart Homo sapiens cDNA clone F801... 101 1e-19  
AA371076, AA371076 EST82846 Prostate gland I Homo sapiens cDN... 42 0.081  
AA977111, AA977111 oq24c03.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 40 0.32  
AA608923, AA608923 af03b04.s1 Soares testis NHT Homo sapiens ... 38 1.3

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gb|AA589082|AA589082 vk24a08.r1 Knowles Solter mouse blastocyst... 658 0.0  
gb|AA510881|AA510881 vh59c11.r1 Soares mouse mammary gland NbMM... 617 e-175  
gb|AA763574|AA763574 vp07e08.r1 Soares mouse mammary gland NbMM... 615 e-174  
gb|AA387423|AA387423 vc84b03.r1 Ko mouse embryo 11 5dpc Mus mus... 549 e-155  
gb|AA915333|AA915333 vz28f05.r1 Soares 2NbMT Mus musculus cDNA ... 543 e-153  
gb|AA816208|AA816208 vp43c10.r1 Barstead mouse irradiated colon... 444 e-123  
gb|AA190043|AA190043 mt91h08.r1 Soares mouse lymph node NbMLN M... 424 e-117  
gb|AA207393|AA207393 mv89c09.r1 GuayWoodford Beier mouse kidney... 394 e-108  
emb|Z31258|MMTEST693 M.musculus expressed sequence tag MTEST693 309 8e-83  
gb|AA930143|AA930143 vz52d11.s1 Soares 2NbMT Mus musculus cDNA ... 293 5e-78  
gb|AA170612|AA170612 ms92c09.r1 Soares mouse 3NbMS Mus musculus... 287 3e-76  
gb|AA762238|AA762238 vw58h02.r1 Soares mouse mammary gland NMLM... 266 1e-69  
gb|AA689028|AA689028 vs02c12.r1 Barstead mouse irradiated colon... 264 4e-69  
gb|AA959938|AA959938 vw58h02.s1 Soares mouse mammary gland NMLM... 240 6e-62  
dbj|D18511|MUSGS01569 Mouse 3'-directed cDNA, MUSGS01569, clon... 172 1e-41  
gb|AA474393|AA474393 vd57g07.r1 Knowles Solter mouse blastocyst... 100 1e-19  
gb|W97165|W97165 mf90g05.r1 Soares mouse embryo NbME13.5 14.5 M... 74 8e-12  
gb|AA512077|AA512077 vj43f05.r1 Stratagene mouse skin (#937313)... 62 3e-08  
gb|AA794521|AA794521 vu68e07.r1 Stratagene mouse skin (#937313)... 54 8e-06  
gb|AA155454|AA155454 mn38h12.r1 Beddington mouse embryonic regi... 48 5e-04  
gb|W91000|W91000 mf83f06.r1 Soares mouse embryo NbME13.5 14.5 M... 40 0.12



gb|AA219917|AA219917 mv62f05.r1 Soares mouse 3NME12 5 Mus muscu... 38 0.45  
 gb|AA529349|AA529349 vi35f08.r1 Beddington mouse embryonic regi... 36 1.8  
 gb|AA754855|AA754855 vu51e08.r1 Soares mouse mammary gland NbMM... 36 1.8

gb|AA850379|AA850379 EST193146 Normalized rat ovary, Bento Soar... 569 e-161  
 gb|W63375|W63375 TgESTzy68g02.r1 TgME49 Tachyzoite cDNA Toxopla... 394 e-108  
 gb|AA946379|AA946379 EST201878 Normalized rat lung, Bento Soare... 353 5e-96  
 gb|AA964427|AA964427 UI-R-E1-gp-a-08-0-UI.s1 UI-R-E1 Rattus nor... 335 1e-90  
 gb|AA849599|AA849599 EST192366 Normalized rat muscle, Bento Soa... 307 3e-82  
 gb|AA849595|AA849595 EST192362 Normalized rat muscle, Bento Soa... 307 3e-82  
 gb|AA850378|AA850378 EST193145 Normalized rat ovary, Bento Soar... 278 3e-73  
 gb|AA957389|AA957389 UI-R-E1-fu-b-04-0-UI.s1 UI-R-E1 Rattus nor... 157 6e-37  
 gb|AI012981|AI012981 EST207432 Normalized rat spleen, Bento Soa... 147 6e-34  
 dbj|C48357|C48357 C.elegans cDNA clone yk469b2 : 5' end, single... 40 0.10  
 gb|AA440444|AA440444 LD15290.5prime LD Drosophila melanogaster ... 36 1.6  
 dbj|C22690|C22690 Rice cDNA, partial sequence (S5274\_4A) 36 1.6  
 gb|AA697626|AA697626 HL02895.5prime HL Drosophila melanogaster ... 36 1.6  
 gb|AA550136|AA550136 1244m3 gmbPfHB3.1, G. Roman Reddy Plasmodi... 36 1.6  
 gb|T43579|T43579 6842 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 1.6  
 gb|AI030501|AI030501 UI-R-C0-jc-g-02-0-UI.s1 UI-R-C0 Rattus nor... 36 1.6  
 gb|AA056876|AA056876 SWMFCA987SK Brugia malayi microfilaria cDN... 36 1.6  
 gb|AA440689|AA440689 LD15550.5prime LD Drosophila melanogaster ... 36 1.6

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emb|Z47552|HSFMO3 H.sapiens mRNA for flavin-containing monooxyg... 44 0.10  
 gb|U39966|HSFMO3G7 Homo sapiens flavin containing monooxygenase... 44 0.10  
 emb|AL021026|HS127D3 Homo sapiens DNA sequence from PAC 127D3 o... 44 0.10  
 gb|U35007|CPU35007 Carcharhinus plumbeus Ig lambda light chain ... 44 0.10  
 gb|U35008|CPU35008 Carcharhinus plumbeus Ig lambda light chain ... 44 0.10  
 dbj|D85068|RICT3A Rice transposable element T3 gene and ret... 42 0.40  
 dbj|D63711|RICT3 Rice transposon T3 DNA, complete sequence 42 0.40  
 gb|U01657|U01657 Carcharhinus plumbeus Ig lambda-chain gene, co... 42 0.40  
 emb|Z92540|HS179I15A Human DNA sequence from PAC 179I15, BRCA2 ... 40 1.6  
 dbj|AB001569|AB001569 Carrot DNA for transposon Tdc1 40 1.6  
 gb|AE000613|HPAE000613 Helicobacter pylori section 91 of 134 of... 40 1.6  
 emb|X07985|DMCUT Drosophila cut locus mRNA for homeodomain-cont... 40 1.6  
 gb|AC005217|AC005217 Homo sapiens chromosome 5, P1 clone 1047D6... 40 1.6

HUMAN ESTs

002050-666966

gb|AA401219|AA401219 zv63a03.r1 Soares total fetus Nb2HF8 9w Ho... 993 0.0  
 gb|H69371|H69371 yu19h09.r1 Homo sapiens cDNA clone 234305 5' s... 44 0.049  
 gb|N62576|N62576 za13d10.s1 Homo sapiens cDNA clone 292435 3' s... 42 0.19  
 gb|W77763|W77763 zd69c06.r1 Soares fetal heart NbHH19W Homo sap... 40 0.77  
 gb|R14832|R14832 yf93g05.r1 Homo sapiens cDNA clone 30203 5'. 40 0.77  
 gb|T90524|T90524 yd40a04.s1 Homo sapiens cDNA clone 110670 3' s... 38 3.0  
 gb|R91887|R91887 yq04c09.r1 Homo sapiens cDNA clone 195952 5'. 38 3.0  
 gb|AA586935|AA586935 nn68h03.s1 NCI\_CGAP\_Lar1 Homo sapiens cDNA... 38 3.0  
 gb|T46987|T46987 yb12a07.s1 Homo sapiens cDNA clone 70932 3' co... 38 3.0  
 gb|AA853975|AA853975 aj51f09.s1 Soares testis NHT Homo sapiens ... 38 3.0  
 gb|T97059|T97059 ye50e01.r1 Homo sapiens cDNA clone 121176 5'. 38 3.0  
 gb|AA883119|AA883119 am15h02.s1 Soares NFL T GBC S1 Homo sapien... 38 3.0  
 gb|AA860074|AA860074 ak45b06.s1 Soares testis NHT Homo sapiens ... 38 3.0  
 gb|AA889618|AA889618 ak28f06.s1 Soares\_testis\_NHT Homo sapiens ... 38 3.0

gb|AA230450|AA230450 mv73c06.r1 Soares mouse 3NME12 5 Mus muscu... 38 1.1  
 gb|AA058041|AA058041 mj58e08.r1 Soares mouse embryo NbME13.5 14... 38 1.1  
 gb|AA152953|AA152953 mq54a03.r1 Soares 2NbMT Mus musculus cDNA ... 38 1.1  
 gb|W34414|W34414 ma98b07.r1 Soares mouse p3NMF19.5 Mus musculus... 38 1.1  
 gb|AA465969|AA465969 ve90c06.s1 Knowles Solter mouse 2 cell Mus... 38 1.1  
 gb|AA261173|AA261173 mz62b11.r1 Soares mouse lymph node NbMLN M... 38 1.1  
 gb|AA238109|AA238109 mw97b05.r1 Soares mouse NML Mus musculus c... 38 1.1  
 dbj|C86549|C86549 Mus musculus fertilized egg cDNA 3'-end seque... 38 1.1  
 gb|AI048677|AI048677 ub29g09.r1 Soares 2NbMT Mus musculus cDNA ... 38 1.1  
 dbj|D77921|MUSC1A08 Mouse embryonal carcinoma F9 cell cDNA, C1A08 38 1.1  
 gb|AA396183|AA396183 vb45e04.r1 Soares mouse lymph node NbMLN M... 38 1.1  
 gb|AA465898|AA465898 vc62f12.s1 Knowles Solter mouse 2 cell Mus... 36 4.3  
 gb|AA041869|AA041869 mj05b12.r1 Soares mouse embryo NbME13.5 14... 36 4.3  
 gb|AA637824|AA637824 vr21f11.r1 Barstead mouse myotubes MPLRB5 ... 36 4.3  
 gb|W82563|W82563 mf05g06.r1 Soares mouse p3NMF19.5 Mus musculus... 36 4.3  
 gb|AA389972|AA389972 vb30e03.r1 Soares mouse lymph node NbMLN M... 36 4.3  
 gb|AA396253|AA396253 vb45f08.r1 Soares mouse lymph node NbMLN M... 36 4.3  
 gb|AA920907|AA920907 vy84f04.r1 Stratagene mouse macrophage (#9... 36 4.3  
 gb|AA517166|AA517166 vh98h05.r1 Barstead mouse myotubes MPLRB5 ... 36 4.3  
 gb|AA433599|AA433599 vf47a05.r1 Soares mouse NbMH Mus musculus ... 36 4.3  
 gb|AA867252|AA867252 vx25c01.r1 Soares 2NbMT Mus musculus cDNA ... 36 4.3  
 dbj|C85619|C85619 Mus musculus fertilized egg cDNA 3'-end seque... 36 4.3  
 gb|AA260277|AA260277 va93g05.r1 Soares mouse 3NME12 5 Mus muscu... 36 4.3  
 gb|AA172548|AA172548 mt04g11.r1 Soares mouse 3NbMS Mus musculus... 36 4.3  
 gb|AA266879|AA266879 mz96a02.r1 Soares mouse lymph node NbMLN M... 36 4.3  
 gb|AA473019|AA473019 vd43e06.r1 Barstead MPLRB1 Mus musculus cD... 36 4.3

gb|R47549|R47549 SW3ICA119SK *Brugia malayi* infective larva cDNA... 40 0.24  
 gb|H32651|H32651 EST107947 Rat PC-12 cells, untreated *Rattus* sp... 38 0.96  
 gb|AA955987|AA955987 UI-R-E1-fb-f-06-0-UI.s1 UI-R-E1 *Rattus* nor... 38 0.96  
 gb|AA819638|AA819638 UI-R-A0-an-f-03-0-UI.s1 UI-R-A0 *Rattus* nor... 38 0.96  
 gb|AI010914|AI010914 EST205365 Normalized rat muscle, Bento Soa... 38 0.96  
 gb|AA893199|AA893199 EST197002 Normalized rat kidney, Bento Soa... 38 0.96  
 gb|AA945176|AA945176 EST200675 Normalized rat liver, Bento Soar... 38 0.96  
 gb|R95272|R95272 SWOvL3CA167SK *Onchocerca volvulus* infective la... 36 3.8  
 gb|AA917208|AA917208 ka05f02.s1 *Onchocerca volvulus* infective l... 36 3.8  
 dbj|C62023|C62023 *C.elegans* cDNA clone yk249d5 : 5' end, single... 36 3.8  
 gb|AI013322|AI013322 EST207997 Normalized rat spleen, Bento Soa... 36 3.8  
 gb|AI043280|AI043280 TENU0920 *T. cruzi* epimastigote normalized ... 36 3.8  
 gb|AI009422|AI009422 EST203873 Normalized rat heart, Bento Soar... 36 3.8  
 gb|AI012655|AI012655 EST207106 Normalized rat placenta, Bento S... 36 3.8  
 dbj|C62878|C62878 *C.elegans* cDNA clone yk296d4 : 5' end, single... 36 3.8  
 gb|AA915818|AA915818 SWOvL3CA1269SK *Onchocerca volvulus* infecti... 36 3.8  
 gb|W00009|W00009 TgESTzy75b07.r1 TgRH Tachyzoite cDNA *Toxoplasma*... 36 3.8  
 gb|AA943503|AA943503 EST199002 Normalized rat brain, Bento Soar... 36 3.8  
 gb|AA956933|AA956933 UI-R-E1-fl-b-08-0-UI.s1 UI-R-E1 *Rattus* nor... 36 3.8  
 gb|H54977|H54977 HHU16a *Sorghum bicolor* cv. TX430 *Sorghum* bicol... 36 3.8

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gb|AC000112|HSAC000112 Human PAC clone DJ149P21, complete seque... 44 0.082  
 gb|U50197|CELF25E2 *Caenorhabditis elegans* cosmid F25E2. 44 0.082  
 dbj|AB007727|AB007727 *Arabidopsis thaliana* genomic DNA, chromos... 44 0.082  
 gb|U02562|BSU02562 *Bacillus subtilis* N-acetylglucosaminidase (l... 42 0.32  
 dbj|D45048|BACORFX *Bacillus subtilis* gene for beta-N-acetylgluc... 42 0.32  
 emb|Z70683|CEF13B12 *Caenorhabditis elegans* cosmid F13B12, compl... 40 1.3  
 emb|AL023828|CEY17G7B *Caenorhabditis elegans* cosmid Y17G7B, com... 40 1.3  
 gb|U39740|CELZC64 *Caenorhabditis elegans* cosmid ZC64. 40 1.3  
 gb|AF006490|AF006490 *Gossypium hirsutum* adenine nucleotide tran... 40 1.3  
 emb|AL010170|PFSC03098 *Plasmodium falciparum* DNA \*\*\* SEQUENCING... 40 1.3  
 gb|U53701|GHU53701 *Gossypium hirsutum* alcohol dehydrogenase 2d ... 40 1.3

#### HUMAN ESTs

gb|AA670455|AA670455 ae62h05.s1 Stratagene lung carcinoma 93721... 852 0.0  
 gb|AA251062|AA251062 zs07c10.r1 NCI\_CGAP\_GCB1 *Homo sapiens* cDNA... 795 0.0

gb|AA669916|AA669916 ag42h08.s1 Jia bone marrow stroma Homo sap... 638 0.0  
 gb|AA300058|AA300058 EST12665 Uterus tumor I Homo sapiens cDNA ... 587 e-165  
 gb|AA664277|AA664277 ac08c05.s1 Stratagene HeLa cell s3 937216 ... 549 e-154  
 gb|AA373224|AA373224 EST85230 HSC172 cells I Homo sapiens cDNA ... 529 e-148  
 gb|AA225705|AA225705 nc10b05.r1 NCI\_CGAP\_Pr1 Homo sapiens cDNA ... 515 e-144  
 gb|W27883|W27883 39b10 Human retina cDNA randomly primed sublib... 484 e-134  
 gb|R24643|R24643 yh36g05.r1 Homo sapiens cDNA clone 131864 5'. 438 e-121  
 gb|N93137|N93137 zb28h06.s1 Homo sapiens cDNA clone 304955 3'. 432 e-119  
 gb|AA250933|AA250933 zs07d01.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 426  
 e-117  
 gb|AA216370|AA216370 nc10b05.s1 NCI\_CGAP\_Pr1 Homo sapiens cDNA ... 398 e-109  
 gb|H26939|H26939 yl64g01.r1 Homo sapiens cDNA clone 163056 5'. 394 e-108  
 gb|H30169|H30169 yo58g09.r1 Homo sapiens cDNA clone 182176 5'. 394 e-108  
 gb|W38854|W38854 zb28h06.r1 Soares parathyroid tumor NbHPA Homo... 359 5e-97  
 gb|AA602297|AA602297 np25a11.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 281 1e-73  
 gb|AA167151|AA167151 zp06e09.r1 Stratagene ovarian cancer (#937... 256 6e-66  
 gb|AA172387|AA172387 zo99d03.s1 Stratagene ovarian cancer (#937... 234 2e-59  
 gb|AA173748|AA173748 zo99d03.r1 Stratagene ovarian cancer (#937... 224 2e-56  
 gb|T83979|T83979 yd66a11.s1 Homo sapiens cDNA clone 113180 3'. 220 3e-55  
 dbj|D61540|HUM415A08B Human fetal brain cDNA 5'-end GEN-415A08. 194 2e-47  
 gb|N45148|N45148 yv25a05.r1 Homo sapiens cDNA clone 243728 5'. 165 2e-38  
 gb|AA642960|AA642960 60f07.s1 NCI\_CGAP\_Lym3 Homo sapiens cDNA... 147 4e-33  
 gb|R90980|R90980 yp93a03.r1 Homo sapiens cDNA clone 194956 5' s... 40 0.62  
 gb|AA521500|AA521500 aa73h08.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.62  
 gb|H82921|H82921 yq46h10.s1 Homo sapiens cDNA clone 198883 3' s... 40 0.62  
 gb|AA294871|AA294871 EST100023 Pancreas tumor I Homo sapiens cD... 38 2.4  
 dbj|D63191|HUM503F11B Human placenta cDNA 5'-end GEN-503F11. 38 2.4  
 gb|AA211096|AA211096 zq89g01.s1 Stratagene hNT neuron (#937233)... 38 2.4

gb|AA840137|AA840137 ud01e08.r1 Soares mouse uterus NMPu Mus mu... 383 e-104  
 gb|AA145994|AA145994 mr13h04.r1 Soares mouse 3NbMS Mus musculus... 345 3e-93  
 gb|AA146365|AA146365 mr05d05.r1 Soares mouse 3NbMS Mus musculus... 236 2e-60  
 gb|AA203902|AA203902 mu60f02.r1 Soares mouse lymph node NbMLN M... 236 2e-60  
 gb|AA204516|AA204516 mu66c10.r1 Soares mouse lymph node NbMLN M... 182 2e-44  
 gb|AA137343|AA137343 mq80g08.r1 Stratagene mouse melanoma (#937... 52 6e-05  
 gb|AA174717|AA174717 ms67a01.r1 Soares mouse 3NbMS Mus musculus... 48 0.001  
 gb|W34073|W34073 ma85d10.r1 Soares mouse p3NMF19.5 Mus musculus... 48 0.001  
 gb|AA289493|AA289493 vb36b01.r1 Soares mouse lymph node NbMLN M... 48 0.001  
 gb|AA177700|AA177700 mt33e12.r1 Soares mouse 3NbMS Mus musculus... 48 0.001  
 gb|AA146021|AA146021 mr13e03.r1 Soares mouse 3NbMS Mus musculus... 48 0.001  
 gb|AA155352|AA155352 mn43d09.r1 Beddington mouse embryonic regi... 46 0.004  
 gb|AA880874|AA880874 vx33b02.r1 Stratagene mouse lung 937302 Mu... 42 0.056

004629-060700

gb|AA590520|AA590520 vi54b08.r1 Beddington mouse embryonic regi... 38 0.88  
gb|AA596629|AA596629 vm56e06.r1 Stratagene mouse Tcell 937311 M... 38 0.88  
dbj|D76657|MUS75H09 Mouse embryonal carcinoma F9 cell cDNA, 75H09 38 0.88  
gb|AA050336|AA050336 mj12f05.r1 Soares mouse embryo NbME13.5 14... 38 0.88  
gb|AA120196|AA120196 mn35a12.r1 Beddington mouse embryonic regi... 38 0.88  
gb|W85267|W85267 mf42c06.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.5  
gb|AA239372|AA239372 my38f03.r1 Barstead mouse pooled organs MP... 36 3.5  
gb|AA497891|AA497891 vi73c07.r1 Stratagene mouse testis (#93730... 36 3.5  
gb|AA673053|AA673053 vn45e05.r1 Barstead mouse myotubes MPLRB5 ... 36 3.5  
emb|Z36324|MM224 M.musculus mRNA (clone 224) for expressed sequ... 36 3.5  
gb|AI021128|AI021128 ub01f06.r1 Soares mouse mammary gland NbMM... 36 3.5  
gb|AA403424|AA403424 mz56f07.r1 Barstead mouse pooled organs MP... 36 3.5  
gb|W66683|W66683 me23g11.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.5  
gb|AA689022|AA689022 vs02c03.r1 Barstead mouse irradiated colon... 36 3.5  
gb|AA574590|AA574590 vn63h11.r1 Barstead mouse proximal colon M... 36 3.5

dbj|C90696|C90696 Dictyostelium discoideum slug cDNA, clone SSJ634 38 0.78  
gb|AA269052|AA269052 MA1MA052.AA3 S. mansoni adult Lambda Zap S... 38 0.78  
gb|AA998786|AA998786 UI-R-C0-im-e-11-0-UI.s1 UI-R-C0 Rattus nor... 38 0.78  
gb|H33464|H33464 EST109494 Rat PC-12 cells, NGF-treated (9 days... 38 0.78  
gb|AA390721|AA390721 LD09459.5prime LD Drosophila melanogaster ... 36 3.1  
dbj|C83908|C83908 Dictyostelium discoideum slug cDNA, clone SSA567 36 3.1  
gb|AA202425|AA202425 LD02606.5prime LD Drosophila melanogaster ... 36 3.1  
gb|AI030951|AI030951 UI-R-C0-jf-d-04-0-UI.s1 UI-R-C0 Rattus nor... 36 3.1  
gb|N60251|N60251 TgESTzy11d04.r1 TgRH Tachyzoite cDNA Toxoplasma... 36 3.1  
gb|AA246875|AA246875 LD05855.5prime LD Drosophila melanogaster ... 36 3.1  
gb|AA803682|AA803682 GM13955.5prime GM Drosophila melanogaster ... 36 3.1  
gb|AA997528|AA997528 UI-R-C0-hw-h-11-0-UI.s1 UI-R-C0 Rattus nor... 36 3.1  
gb|AA695197|AA695197 GM02389.5prime GM Drosophila melanogaster ... 36 3.1  
gb|AA567339|AA567339 HL01077.5prime HL Drosophila melanogaster ... 36 3.1  
gb|AA950648|AA950648 LD30547.5prime LD Drosophila melanogaster ... 36 3.1

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substantially identical to D86956

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gb|AC004505|AC004505 Homo sapiens chromosome 20, P1 clone 86C1 ... 176 1e-41  
 gb|S78798|S78798 1-phosphatidylinositol-4-phosphate 5-kinase is... 115 4e-23  
 gb|U48696|HSU48696 Human mariner-like element-containing mRNA, ... 115 4e-23  
 gb|U66300|LEU66300 Lycopersicon esculentum heat shock protein (... 115 4e-23  
 gb|AF045432|AF045432 Danio rerio stem cell leukemia protein (ta... 111 6e-22  
 emb|Z97178|BVRNAEF2 Beta vulgaris cDNA for elongation factor 2 107 9e-21  
 gb|U39066|MMU39066 Murine MAP kinase kinase 6c mRNA, complete cds. 101 6e-19  
 gb|U37573|XXU37573 Shuttle expression vector pBKCMV. 96 4e-17  
 gb|AF033097|AF033097 Avena sativa nonphototropic hypocotyl 1 (N... 90 2e-15  
 gb|AF027174|AF027174 Arabidopsis thaliana cellulose synthase ca... 86 3e-14  
 gb|U65376|CFU65376 Canis familiaris rod photoreceptor transduci... 84 1e-13  
 gb|AF033565|AF033565 Mus musculus cdc2/CDC28-like protein kinas... 82 5e-13  
 emb|Z49980|HS2AMCP H.sapiens mRNA for ets-like protein (clone 7... 82 5e-13  
 emb|AJ001103|LLARCAB Lactococcus lactis arcA and arcB genes 80 2e-12  
 gb|U52868|CFU52868 Canis familiaris retinal cyclic-GMP phosphod... 80 2e-12  
 gb|G29058|G29058 chicken STS ADL368 76 3e-11  
 gb|G29060|G29060 chicken STS ADL352 76 3e-11  
 gb|U34048|HDU34048 Haemophilus ducreyi hemoglobin-binding prote... 76 3e-11  
 gb|U44386|SLU44386 Solanum lycopersicum heat shock protein (TFH... 68 8e-09  
 gb|S83098|S83098 ribosomal protein S3 [Ambystoma mexicanum=Mexi... 66 3e-08  
 gb|U48697|HSU48697 Human mariner-like element-containing mRNA, ... 60 2e-06  
 gb|AF033096|AF033096 Avena sativa nonphototropic hypocotyl 1 (N... 60 2e-06  
 emb|X99051|LLATTMSAT L.lagopus ATT microsatellite, locus LLST1 58 8e-06  
 gb|U41811|HAU41811 Homarus americanus beta-I tubulin mRNA, comp... 46 0.029  
 emb|X99055|LLCAMSAT1 L.lagopus CA microsatellite, locus LLS5 44 0.12  
 emb|X65215|BTMISATN B.taurus microsatellite DNA (624bp) 44 0.12  
 gb|AE001023|AE001023 Archaeoglobus fulgidus section 84 of 172 o... 42 0.46  
 emb|X80164|HSPDCM4 H.salinarium phage dcm4 Virus DNA 42 0.46  
 emb|X87859|MTCMAJ12S C.major mitochondrial gene for 12S ribosom... 42 0.46  
 emb|X87861|MTCPAL12S C.pallidus mitochondrial gene for 12S ribo... 42 0.46  
 gb|L13767|STMSEC101A Streptomyces lividans sec101 gene, 5' end p... 42 0.46  
 emb|Y08962|OSTRAMBPR O.sativa mRNA for transmembrane protein >g... 40 1.8  
 gb|S65686|S65686 {multiple cloning sites, vector} [bacteriophag... 40 1.8  
 gb|J02871|HUMCP45IV Human lung cytochrome P450 (IV subfamily) B... 40 1.8  
 dbj|D10450|HUMRTVE Human genomic DNA, retrovirus-like element 40 1.8  
 gb|S65683|S65683 {multiple cloning sites, vector} [bacteriophag... 40 1.8  
 gb|L14950|PIGALDRED Sus scrofa aldose reductase mRNA, complete ... 40 1.8  
 gb|S65693|S65693 {multiple cloning sites, vector} [bacteriophag... 40 1.8  
 gb|S65694|S65694 {multiple cloning sites, vector} [bacteriophag... 40 1.8  
 emb|AJ223292|SPAJ3292 Streptococcus pyogenes SOD gene, complete... 40 1.8  
 gb|U25846|HAU25846 Homarus americanus clone LOB5 farnesoic acid... 40 1.8  
 emb|X16699|HSP450P2 Human mRNA for cytochrome P-450HP 40 1.8  
 gb|U37100|HSU37100 Homo sapiens aldose reductase-like peptide m... 40 1.8

## HUMAN ESTs

gb|AA305996|AA305996 EST177003 Jurkat T-cells VI Homo sapiens c... 942 0.0  
 gb|AA975279|AA975279 oq36e08.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 900 0.0  
 gb|AA426359|AA426359 zw11b02.r1 Soares NhHMPu S1 Homo sapiens c... 868 0.0  
 gb|AA424296|AA424296 zv90b08.r1 Soares NhHMPu S1 Homo sapiens c... 749 0.0  
 gb|AA632259|AA632259 np67d04.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 730 0.0  
 gb|H80377|H80377 yu59e01.r1 Homo sapiens cDNA clone 230424 5'. 658 0.0  
 gb|AA515175|AA515175 ng68f10.s1 NCI\_CGAP\_Lip2 Homo sapiens cDNA... 615 e-174  
 gb|AA351770|AA351770 EST59616 Infant brain Homo sapiens cDNA 5'... 611 e-172  
 gb|AA426522|AA426522 zw11b02.s1 Soares NhHMPu S1 Homo sapiens c... 587 e-165  
 gb|AA676220|AA676220 zi22a12.s1 Soares fetal liver spleen 1NFLS... 585 e-165  
 gb|R35132|R35132 yg60e09.r1 Homo sapiens cDNA clone 36874 5'. 579 e-163  
 gb|H80280|H80280 yu59e01.s1 Homo sapiens cDNA clone 230424 3'. 579 e-163  
 gb|H81145|H81145 yu60e01.r1 Homo sapiens cDNA clone 230520 5'. 561 e-157  
 gb|AA311105|AA311105 EST18187 Heart I Homo sapiens cDNA 5' end 533 e-149  
 gb|AA380530|AA380530 EST93691 Supt cells Homo sapiens cDNA 5' end 527 e-147  
 gb|H81050|H81050 yu60e01.s1 Homo sapiens cDNA clone 230520 3'. 500 e-139  
 gb|AA460005|AA460005 zx49g07.s1 Soares testis NHT Homo sapiens ... 482 e-134  
 gb|AA076450|AA076450 zm91d12.r1 Stratagene ovarian cancer (#937... 466 e-129  
 gb|N43873|N43873 yy43e09.r1 Homo sapiens cDNA clone 274024 5'. 452 e-125  
 gb|AA076451|AA076451 zm91d12.s1 Stratagene ovarian cancer (#937... 418 e-115  
 gb|AA907095|AA907095 ol03b12.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 414 e-113  
 gb|W01027|W01027 za56g07.r1 Soares fetal liver spleen 1NFLS Hom... 262 1e-67  
 gb|AA127183|AA127183 zn29d11.r1 Stratagene neuroepithelium NT2R... 222 1e-55  
 gb|H65491|H65491 yr56a08.s1 Homo sapiens cDNA clone 209270 3'. 222 1e-55  
 gb|N48543|N48543 yy49d08.r1 Homo sapiens cDNA clone 276879 5'. 210 4e-52  
 gb|R32579|R32579 yh54h06.r1 Homo sapiens cDNA clone 133595 5'. 194 2e-47  
 gb|AA247827|AA247827 j0778.seq.F Human fetal heart, Lambda ZAP ... 117 5e-24  
 N84048, (many others similar, but smaller)

gb|AA589598|AA589598 vl49d08.s1 Stratagene mouse skin (#937313)... 398 e-109  
 gb|AA647465|AA647465 vq82f02.s1 Knowles Solter mouse 2 cell Mus... 385 e-105  
 gb|AA510284|AA510284 vh58f02.r1 Soares mouse mammary gland NbMM... 345 4e-93  
 gb|AA028696|AA028696 mil2e12.r1 Soares mouse p3NMF19.5 Mus musc... 307 9e-82  
 gb|N28081|N28081 MDB1409R Mouse brain, Stratagene Mus musculus ... 244 1e-62  
 gb|AA177452|AA177452 mt24c12.r1 Soares mouse 3NbMS Mus musculus... 226 3e-57  
 gb|N28080|N28080 MDB1409 Mouse brain, Stratagene Mus musculus c... 226 3e-57  
 dbj|C88310|C88310 Mus musculus fertilized egg cDNA 3'-end seque... 226 3e-57  
 gb|AA763786|AA763786 vo99g12.r1 Soares mouse mammary gland NbMM... 94 2e-17  
 gb|AA667535|AA667535 vv18b12.r1 Stratagene mouse heart (#937316... 40 0.31  
 gb|AA208274|AA208274 mv96a01.r1 GuayWoodford Beier mouse kidney... 38 1.2

gb|AA444814|AA444814 vg50e04.r1 Soares mouse mammary gland NbMM... 38 1.2  
 gb|AA763341|AA763341 vw53b12.r1 Soares mouse mammary gland NMLM... 38 1.2  
 gb|AA110827|AA110827 mp57a12.r1 Soares 2NbMT Mus musculus cDNA ... 38 1.2  
 gb|AA691932|AA691932 vt06b04.r1 Barstead mouse myotubes MPLRB5 ... 38 1.2  
 gb|W77233|W77233 me61f11.r1 Soares mouse embryo NbME13.5 14.5 M... 38 1.2  
 gb|AA072872|AA072872 mm80g08.r1 Stratagene mouse embryonic carc... 38 1.2  
 gb|AA980630|AA980630 ua43f05.r1 Soares mouse mammary gland NbMM... 36 4.9  
 gb|AA065522|AA065522 ml54d09.r1 Stratagene mouse testis (#93730... 36 4.9  
 gb|AA982398|AA982398 uh07b08.r1 Soares mouse hypothalamus NMHy ... 36 4.9  
 gb|W62610|W62610 md58c06.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.9  
 gb|AA286651|AA286651 vb79b02.r1 Soares mouse 3NME12 5 Mus muscu... 36 4.9  
 gb|AA399772|AA399772 vd70g05.r1 Beddington mouse embryonic regi... 36 4.9  
 gb|AA510475|AA510475 vg32h08.r1 Soares mouse mammary gland NbMM... 36 4.9  
 gb|AA109064|AA109064 ml63g02.r1 Stratagene mouse testis (#93730... 36 4.9  
 gb|AA033485|AA033485 mi42c08.r1 Soares mouse embryo NbME13.5 14... 36 4.9  
 gb|W57221|W57221 md59g10.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.9  
 gb|AA467106|AA467106 vd98b04.r1 Soares mouse NbMH Mus musculus ... 36 4.9  
 gb|W97470|W97470 mf95a11.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.9  
 gb|AA606917|AA606917 vm91c05.r1 Knowles Solter mouse blastocyst... 36 4.9  
 dbj|C78330|C78330 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 36 4.9  
 gb|AA013753|AA013753 mh26h12.r1 Soares mouse placenta 4NbMP13.5... 36 4.9  
 gb|AA145240|AA145240 mr12a03.r1 Soares mouse 3NbMS Mus musculus... 36 4.9  
 gb|AA245533|AA245533 mx03c11.r1 Soares mouse NML Mus musculus c... 36 4.9  
 gb|AA770893|AA770893 vt13a08.r1 Barstead mouse myotubes MPLRB5 ... 36 4.9  
 dbj|C79987|C79987 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 36 4.9  
 gb|AA014027|AA014027 mh24a12.r1 Soares mouse placenta 4NbMP13.5... 36 4.9  
 dbj|C89051|C89051 Mus musculus early blastocyst cDNA, clone 01B... 36 4.9  
 gb|AA058308|AA058308 mj59e09.r1 Soares mouse embryo NbME13.5 14... 36 4.9  
 gb|AA673826|AA673826 vu08h10.r1 Barstead mouse myotubes MPLRB5 ... 36 4.9  
 gb|AA637080|AA637080 vn07h04.r1 Knowles Solter mouse blastocyst... 36 4.9  
 gb|W44292|W44292 mc80c07.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.9

gb|AA955972|AA955972 UI-R-E1-ff-d-10-0-UI.s1 UI-R-E1 Rattus nor... 159 4e-37  
 gb|AA957275|AA957275 UI-R-E1-fq-f-08-0-UI.s1 UI-R-E1 Rattus nor... 157 2e-36  
 emb|Z84031|SSZ84031 S.scrofa mRNA; expressed sequence tag (5'; ... 111 9e-23  
 gb|AF041408|AF041408 Fragaria x ananassa clone FA110b 96 5e-18  
 gb|AA933116|AA933116 SWBmL3SA048T3 Brugia malayi L3 subtracted ... 58 1e-06  
 gb|AA933363|AA933363 SWBmL3SA615T3 Brugia malayi L3 subtracted ... 52 7e-05  
 gb|AA660164|AA660164 00001 MtrHE Medicago truncatula cDNA 5' si... 50 3e-04  
 gb|N37420|N37420 18647 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 44 0.018  
 gb|H35981|H35981 14503 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 44 0.018  
 gb|AA882627|AA882627 TENS0198 T. cruzi epimastigote normalized ... 44 0.018  
 gb|AI026481|AI026481 TENU0693 T. cruzi epimastigote normalized ... 42 0.070  
 gb|AA946369|AA946369 EST201868 Normalized rat lung, Bento Soare... 42 0.070



gb|AI010371|AI010371 EST204822 Normalized rat lung, Bento Soare... 42 0.070  
 gb|AI010257|AI010257 EST204708 Normalized rat lung, Bento Soare... 42 0.070  
 dbj|D39318|RICR3325A Rice cDNA, partial sequence (R3325\_1A). 40 0.28  
 gb|U40140|OSU40140 Oryza sativa clone pFDRRC22 mRNA sequence. 40 0.28  
 gb|AI009132|AI009132 EST203583 Normalized rat embryo, Bento Soa... 40 0.28  
 dbj|D47291|RICS12574A Rice cDNA, partial sequence (S12574\_1A). 40 0.28  
 dbj|D47316|RICS12613A Rice cDNA, partial sequence (S12613\_1A). 40 0.28  
 gb|T42265|T42265 5528 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 40 0.28  
 dbj|D47631|RICS13239A Rice cDNA, partial sequence (S13239\_1A). 40 0.28  
 gb|AI013513|AI013513 EST208188 Normalized rat spleen, Bento Soa... 40 0.28  
 gb|AA751980|AA751980 96AS0896 Rice Immature Seed Lambda ZAPII c... 40 0.28  
 gb|AA660165|AA660165 00002 MtrHE Medicago truncatula cDNA 5' si... 40 0.28  
 emb|Z34868|ATTS3597 A. thaliana transcribed sequence; clone FAF... 40 0.28  
 dbj|D39131|RICR2302A Rice cDNA, partial sequence (R2302\_1A). 40 0.28  
 gb|AA963968|AA963968 UI-R-C0-gs-b-05-0-UI.s1 UI-R-C0 Rattus nor... 40 0.28  
 gb|AA866346|AA866346 UI-R-A0-bm-a-05-0-UI.s1 UI-R-A0 Rattus nor... 40 0.28  
 gb|AI044437|AI044437 UI-R-C1-js-e-06-0-UI.s1 UI-R-C1 Rattus nor... 40 0.28  
 dbj|D41811|RICS4634A Rice cDNA, partial sequence (S4634\_1A). 40 0.28  
 dbj|C19261|C19261 Rice cDNA, partial sequence (E10176\_1A) 40 0.28  
 dbj|D48409|RICS14588A Rice cDNA, partial sequence (S14588\_1A). 40 0.28  
 dbj|C26556|C26556 Rice cDNA, partial sequence (C12586\_1A) 40 0.28  
 dbj|D47831|RICS13548A Rice cDNA, partial sequence (S13548\_1A). 40 0.28  
 dbj|C72152|C72152 Rice cDNA, partial sequence (E1094\_3A) 40 0.28  
 dbj|D46553|RICS11305A Rice cDNA, partial sequence (S11305\_2A). 40 0.28  
 gb|AI028926|AI0289 (and many others of similar score)

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emb|X68308|OOLPLIP O.ovis mRNA for lipoprotein lipase 40 1.2  
 gb|AE000660|HUA000660 Homo sapiens T-cell receptor alpha delta... 40 1.2  
 emb|AL022333|HS474I12 Human DNA sequence \*\*\* SEQUENCING IN PROG... 38 4.6  
 emb|Z12618|CFTRG C.fasciculata gene encoding trypanothione redu... 38 4.6  
 gb|M81651|HUMSEMIIB Human semenogelin II (SEMGII) gene, complet... 38 4.6  
 gb|M96980|HUMMYT1A Homo sapiens myelin transcription factor 1 (... 38 4.6  
 gb|U89688|ACU89688 Acanthamoeba castellanii myosin-I binding pr... 38 4.6  
 gb|AC002497|AC002497 Human Cosmid g1940a142 from 7q31.3, comple... 38 4.6  
 gb|M81652|HUMSMNGLN Homo sapiens semenogelin II mRNA, complete ... 38 4.6  
 gb|M25665|HUMNCF1A Human neutrophil cytosol factor 1 (NCF-47k) ... 38 4.6  
 gb|M73325|TRFTRPREDC Crithidia fasciculata trypanothione reduct... 38 4.6  
 gb|M73324|TRFTRPREDB Crithidia fasciculata trypanothione reduct... 38 4.6  
 emb|X92589|MMSEMIIGN M.mulatta semenogelin II gene 38 4.6  
 emb|Z47556|HSSG1SG2 H.sapiens genes for semenogelin I and semen... 38 4.6  
 gb|AC004753|AC004753 Homo sapiens chromosome 16, cosmid clone R... 38 4.6  
 gb|M55067|HUMNADPHO Human 47-kD autosomal chronic granulomatous... 38 4.6

gb|M73323|TRFTRPRED A Crithidia fasciculata trypanothione reduct... 38 4.6

# HUMAN ESTs

gb|R11942|R11942 yf54c05.r1 Homo sapiens cDNA clone 25950 5'. 656 0.0  
 gb|AA366384|AA366384 EST77326 Pancreas tumor III Homo sapiens c... 470 e-130  
 gb|T12566|T12566 CHR90086 Homo sapiens genomic clone P94\_24 5' ... 133 5e-29  
 gb|R37032|R37032 yf54c05.s1 Homo sapiens cDNA clone 25950 3'. 44 0.036  
 gb|AA661650|AA661650 nv02h12.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA261982|AA261982 zs20d03.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 38 2.2  
 gb|AA588219|AA588219 no24c11.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA250891|AA250891 zs06c06.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 38 2.2  
 gb|AA244177|AA244177 nc05a02.r1 NCI\_CGAP\_Pr1 Homo sapiens cDNA ... 38 2.2  
 gb|AA715147|AA715147 nv10d05.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA659887|AA659887 nv03a10.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA627890|AA627890 nq70a08.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA603596|AA603596 np27b11.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA613738|AA613738 np25h09.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA715248|AA715248 nv10h06.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AI038487|AI038487 ow25d12.x1 Soares parathyroid tumor\_NbHPA ... 38 2.2  
 gb|AA252786|AA252786 zs26f10.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 38 2.2  
 gb|AA287819|AA287819 zs50h04.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 38 2.2  
 gb|AA564176|AA564176 nj04c08.s1 NCI\_CGAP\_Pr21 Homo sapiens cDNA... 38 2.2  
 gb|AA643870|AA643870 np26h07.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA280371|AA280371 zt05f07.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 38 2.2  
 gb|R00687|R00687 ye78h08.r1 Homo sapiens cDNA clone 123903 5' s... 38 2.2  
 gb|AA587820|AA587820 nj06h05.s1 NCI\_CGAP\_Pr21 Homo sapiens cDNA... 38 2.2  
 gb|AA588443|AA588443 no22c11.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA568385|AA568385 nl88f06.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 38 2.2  
 gb|AA281831|AA281831 zt06c08.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 38 2.2  
 gb|AA700438|AA700438 zj74b08.s1 Soares fetal liver spleen 1NFLS... 38 2.2  
 gb|AA689530|AA689530 ns66e07.r1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA688300|AA688300 nv14a09.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA687962|AA687962 nv13h04.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA526586|AA526586 ni96f11.s1 NCI\_CGAP\_Pr21 Homo sapiens cDNA... 38 2.2  
 gb|AA642589|AA642589 nq73f04.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA541594|AA541594 ni89g07.s1 NCI\_CGAP\_Pr21 Homo sapiens cDNA... 38 2.2  
 gb|AA278713|AA278713 zs76h02.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 38 2.2  
 gb|T58661|T58661 ya94a07.r1 Homo sapiens cDNA clone 69300 5' si... 38 2.2  
 gb|AA689473|AA689473 ns66e07.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 2.2  
 gb|AA459023|AA459023 aa26a09.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 38 2.2

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004529-06700

dbj|C76752|C76752 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 60 2e-07  
gb|AA123048|AA123048 mn32g01.r1 Beddington mouse embryonic regi... 36 3.2  
gb|AA616529|AA616529 vo10e01.r1 Barstead mouse myotubes MPLRB5 ... 36 3.2  
gb|AA254370|AA254370 va13h09.r1 Soares mouse lymph node NbMLN M... 36 3.2  
gb|AA537288|AA537288 vk46c04.r1 Soares mouse mammary gland NbMM... 36 3.2  
gb|AA462365|AA462365 vg74c05.r1 Soares mouse NbMH Mus musculus ... 36 3.2  
gb|AA589462|AA589462 vl47g07.s1 Stratagene mouse skin (#937313)... 36 3.2  
gb|AA968017|AA968017 uh06h10.r1 Soares mouse hypothalamus NMHy ... 36 3.2

dbj|C93868|C93868 Dictyostelium discoideum slug cDNA, clone SSL809 36 2.8  
gb|AA531984|AA531984 TgESTzz46b06.r1 TgME49 invivo Bradyzoite c... 36 2.8  
gb|N60418|N60418 TgESTzy07a10.r1 TgRH Tachyzoite cDNA Toxoplasm... 36 2.8  
gb|H32045|H32045 EST106774 Rat PC-12 cells, untreated Rattus sp... 36 2.8  
gb|AA956789|AA956789 UI-R-E1-fr-h-01-0-UI.s1 UI-R-E1 Rattus nor... 36 2.8  
gb|H33275|H33275 EST109117 Rat PC-12 cells, NGF-treated (9 days... 36 2.8  
gb|AA531938|AA531938 TgESTzz45b08.r1 TgME49 invivo Bradyzoite c... 36 2.8  
dbj|D41507|RICS4044A Rice cDNA, partial sequence (S4044\_1A). 36 2.8  
gb|AA799411|AA799411 EST188908 Normalized rat heart, Bento Soar... 36 2.8  
gb|AA519671|AA519671 TgESTzz27c10.r1 TgME49 invivo Bradyzoite c... 36 2.8  
dbj|D40678|RICS2786A Rice cDNA, partial sequence (S2786\_1A). 36 2.8  
gb|AA012430|AA012430 TgESTzz22b12.r1 TgME49cDNA Toxoplasma gond... 36 2.8  
dbj|D40551|RICS2612A Rice cDNA, partial sequence (S2612\_1A). 36 2.8  
gb|AI008452|AI008452 EST202903 Normalized rat embryo, Bento Soa... 36 2.8  
dbj|D41253|RICS3620A Rice cDNA, partial sequence (S3620\_1A). 36 2.8  
gb|AA923843|AA923843 UI-R-A1-dr-f-04-0-UI.s1 UI-R-A1 Rattus nor... 36 2.8  
gb|AA799410|AA799410 EST188907 Normalized rat heart, Bento Soar... 36 2.8

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